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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07C 271/36, 271/64, A61K 31/325, 31/33 — A1

(11) International Publication Number: WO 97/25309

(43) International Publication Date: 17 July 1997 (17.07.97)

(21) International Application Number: PCT/EP96/05874

(22) International Filing Date: 19 December 1996 (19.12.96)

(30) Priority Data:

9600048.4	3 January 1996 (03.01.96)	GB
9616305.0	2 August 1996 (02.08.96)	GB

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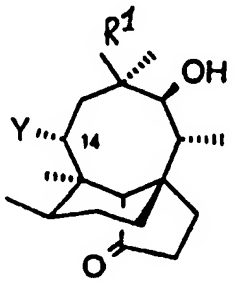
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: CARBAMOYLOXY DERIVATIVES OF MUTILINE AND THEIR USE AS ANTIBACTERIALS

(57) Abstract

Derivatives of mutiline of formula (1A) and pharmaceutically acceptable salts and derivatives thereof, in which R^1 is ethyl or vinyl, Y is a carbamoyloxy group, in which the N-atom is unsubstituted, or mono- or di-substituted, are useful in the treatment of bacterial infections.



(1A)

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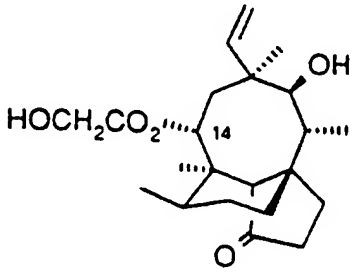
CARBAMOYLOXY DERIVATIVES OF MUTILINE AND THEIR USE AS ANTIBACTERIALS.

The present invention relates to novel compounds, to processes for their preparation, to pharmaceutical compositions containing them and to their use in medical therapy, particularly antibacterial therapy.

Pleuromutilin, the compound of formula (1), is a naturally occurring antibiotic which has antimycoplasmal activity and modest antibacterial activity. It has been shown that the antimicrobial activity can be improved by replacing the glycolic ester moiety at position 14 by an R-X-CH_2CO_2- group, where R is an aliphatic or aromatic moiety and X is O, S, or NR' (H Egger and H Reinshagen, *J Antibiotics*, 1976, 29, 923). Tiamulin, the compound of formula (2), which is used as a veterinary antibiotic, is a derivative of this type (G Hogenauer in *Antibiotics*, Vol. V, part 1, ed. F E Hahn, Springer-Verlag, 1979, p.344).



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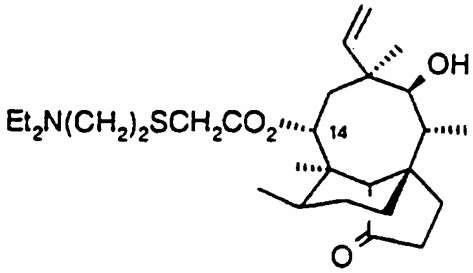


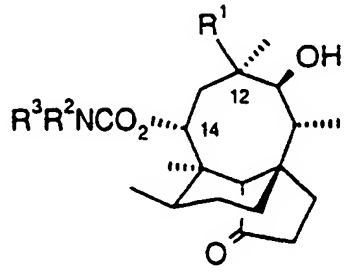
(2)

In this application, the non-conventional numbering system which is generally used in the literature (G Hogenauer, *loc.cit.*) is used.

We have found that pleuromutilin analogues containing a 14-*O*-carbamoyl group, also have improved antimicrobial properties.

Accordingly, in its broadest aspect, the present invention provides a 14-*O*-carbamoyl derivative of mutilin or 19, 20-dihydromutilin, in which the N-atom of the carbamoyl group is unsubstituted, mono- or di-substituted.

More specifically, this invention provides a compound of general formula (3)



(3)

in which:

R^1 is vinyl or ethyl;

R^2 and R^3 are the same or different groups selected from

hydrogen;

a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group;

a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group;

an optionally substituted heterocyclic group;

an optionally substituted aryl group;

or together form an optionally substituted cyclic group of 3 to 8 ring atoms, optionally containing one additional heteroatom selected from N, O and S, and optionally fused to a hydrocarbon ring, a heterocyclic group or an aromatic group; or

R^2 is one of the above monovalent groups and R^3 is a group selected from SO_2R^4, COR^5, OR^5 and NR^6R^7 where

But $R^5 \neq$ N chain.

R^4 is selected from a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group; a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group; an optionally substituted heterocyclic group; an optionally substituted aryl group; an optionally substituted C_1 to C_6 alkyl amino group; and an optionally substituted aryl amino group;

R^5 is selected from hydrogen; a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group; a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group; an optionally substituted heterocyclic group; and an optionally substituted aryl group;

R^6 and R^7 are the same or different groups selected from hydrogen; a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group; a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group; an optionally substituted heterocyclic group, and an optionally substituted aryl group; or together form an optionally substituted cyclic group of 3 to 8 ring atoms, optionally containing one additional heteroatom selected from N, O and S, and optionally fused to a hydrocarbon ring, a heterocyclic group or an aromatic group.

Suitable C_1 to C_6 hydrocarbon groups include straight and branched chain alkyl groups having from 1 to 6 carbon atoms, for instance methyl, ethyl, *n*-propyl and *iso*-propyl, preferably methyl.

Suitable C_3 to C_8 cyclic hydrocarbon groups include cyclopropyl, cyclopentyl and cyclohexyl. cyclo butyl not mentioned

Suitable optional substituents for the (C_{1-6})alkyl groups and the (C_{3-8})cycloalkyl groups include, for example, halogen, hydroxy, (C_{1-6})alkoxy, aryloxy, carboxy and salt thereof, (C_{1-6})alkoxycarbonyl, carbamoyl, mono- or di(C_{1-6})alkylcarbamoyl, sulphamoyl, mono- and di(C_{1-6})alkylsulphamoyl, amino, mono- and di(C_{1-6})alkylamino, (C_{1-6})acylamino, ureido, (C_{1-6})alkoxycarbonylamino, aryl, heterocyclyl, oxo, hydroxyimino, acyl, (C_{1-6})alkylthio, arylthio, (C_{1-6})alkane-sulphinyl, arylsulphinyl, (C_{1-6})alkanesulphonyl, arylsulphonyl.

When used herein, the term "aryl" includes phenyl and naphthyl. Suitably an aryl group, including phenyl and naphthyl, may be optionally substituted by up to five, preferably up to three substituents. Suitable substituents include halogen, (C_{1-6})alkyl, aryl(C_{1-4})alkyl, (C_{1-6})alkoxy, (C_{1-6})alkoxy(C_{1-6})alkyl, halo(C_{1-6})alkyl, hydroxy, nitro, amino, mono- and di-*N*-(C_{1-6})alkylamino,

acylamino, acyloxy, carboxy, carboxy salts, carboxy esters, carbamoyl, mono- and di-*N*-(C_{1-6})alkylcarbamoyl, (C_{1-6})alkoxycarbonyl, aryloxycarbonyl, ureido, guanidino, sulphonylamino, aminosulphonyl, (C_{1-6})alkylthio, (C_{1-6})alkyl sulphinyl (C_{1-6})alkylsulphonyl, heterocyclyl and heterocyclyl (C_{1-4})alkyl. In addition, two adjacent ring carbon atoms may be linked by a (C_{3-5})alkylene chain, to form a carbocyclic ring.

When used herein, the term "heteroaryl" includes aromatic single and fused rings containing up to four heteroatoms in each ring, each of which is selected from oxygen, nitrogen and sulphur, which rings may be unsubstituted or substituted by, for example, up to three substituents. Each heteroaryl ring suitably has 5 or 6 ring atoms. A fused heteroaryl ring may include carbocyclic rings and need include only one heteroaryl ring.

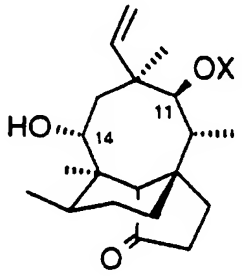
When used herein the terms "heterocyclyl" and "heterocyclic" suitably include, unless otherwise defined, aromatic and non-aromatic, single and fused, rings suitably containing up to four heteroatoms in each ring, each of which is selected from oxygen, nitrogen and sulphur, which rings, may be unsubstituted or substituted by, for example, up to three substituents. Each heterocyclic ring suitably has from 4 to 7, preferably 5 or 6, ring atoms. A fused heterocyclic ring system may include carbocyclic rings and need include only one heterocyclic ring.

Preferably a substituent for a heteroaryl or a heterocyclyl group is selected from halogen, (C_{1-6})alkyl, aryl(C_{1-4})alkyl, (C_{1-6})alkoxy, (C_{1-6})alkoxy(C_{1-6})alkyl, halo(C_{1-6})alkyl, hydroxy, amino, mono- and di-*N*-(C_{1-6})alkyl-amino, acylamino, carboxy salts, carboxy esters, carbamoyl, mono- and di-*N*-(C_{1-6})alkylcarbonyl, aryloxycarbonyl, (C_{1-6})alkoxycarbonyl(C_{1-6})alkyl, aryl, oxy groups, ureido, guanidino, sulphonylamino, aminosulphonyl, (C_{1-6})alkylthio, (C_{1-6})alkylsulphinyl, (C_{1-6})alkylsulphonyl, heterocyclyl and heterocyclyl(C_{1-4})alkyl.

Particularly suitable values for R^2 and R^3 are hydrogen, hydroxy, methoxy, phenyl, methyl, *iso*-propyl, phenylsulphonyl, methoxyphenyl, nitrophenyl, trichloroacetyl, benzyl, hydroxyiminobenzyl, benzylamino-sulfonyl,

dichloropyridinyl, hydroxyethyl, 2-phenylethyl, 1-(R)-phenyl-2-hydroxyethyl, 2-(methoxycarbonyl)ethyl, 2-carboxyethyl, dimethylamino, dimethylaminopropyl, methanesulphonylamino, methanesulphonyl, benzoylamino, benzoyl optionally substituted by trifluoromethyl, carboxy, methoxy, hydroxy, acetoxy, amino or nitro, furoyl, nicotinoyl, *iso*nicotinoyl, acetyl, phenylacetyl, and phenoxy. Particularly suitable values for cyclic groups R^2R^3N are indolino and morpholino.

In a further aspect the present invention provides a method for preparing compounds of the invention, which comprises reacting a compound of formula (4) where X is hydrogen or a hydroxyl protecting group, such as an acyl group, or a compound of formula (5) with an appropriately substituted carbamate-forming reagent.



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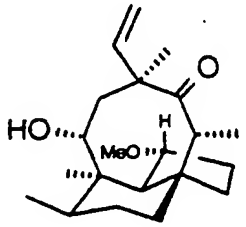


(5)

General methods for preparing carbamates are described, for example, by A F Hegarty in *Comprehensive Organic Chemistry*, Vol. 2, ed. I O Sutherland, Pergamon Press, 1979, p.1083. Typical procedures are reaction with an isocyanate or a carbamoyl chloride, or reaction with phosgene or a phosgene equivalent followed by reaction with an amine.

More particularly, in one aspect the present invention provides a process for the preparation of a compound of formula (3) which comprises reacting a compound of formula (4) in which X is hydrogen or a hydroxyl protecting group, with

(a) a compound R^2 NCO,

(b) a compound R^2R^3NCOCl, or

(c) phosgene or a chloroformate or a carbonate followed by a compound R^2R^3NH,

where R^2 and R^3 are as defined above and are protected where appropriate, and where necessary deprotecting the group X to generate a hydroxyl group at position 11, deprotecting a protected group R^2 or R^3, converting one group R^2 or R^3 to another group R^2 or R^3, or hydrogenating the vinyl group at position 12 to form an ethyl group.

Although in principle it may be possible to prepare compounds of formula (3) by reaction at the 14-hydroxyl in the known compound mutilin (X = H in formula (4)), in practice it is desirable to use an intermediate in which the 11-hydroxyl is protected.

Suitable compounds as formula (4) are

11-*O*-acyl mutilin derivatives, *e.g.* mutilin 11-acetate (X = Ac in formula (4)) (A J Birch, C W Holzapfel, R W Richards, *Tetrahedron (Suppl.)*, 1966, 8, Part II, 359). After formation of the 14-O-carbamoyl derivative, the 11-*O*-acyl group may be removed by selective hydrolysis (*e.g.* using NaOH in MeOH);

In another aspect, the present invention provides a process for the preparation of a compound of formula (3) which comprises reacting a compound of formula (5), with

(a) a compound R^2NCO,

(b) a compound R^2R^3NCOCl, or

(c) phosgene or a chloroformate or a carbonate followed by a compound R^2R^3NH,

where R^2 and R^3 are as defined above and are protected where appropriate, treating the product with acid, deprotecting a protected group R^2 or R^3, converting one group R^2 or R^3 to another group R^2 or R^3, or hydrogenating the vinyl group at position 12 to form an ethyl group.

Formula (5) is

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (H Berner, G Schulz and H Schneider, *Tetrahedron*, 1980, 36, 1807). After

formation of the 14-carbamate , the intermediate may be converted into (3) by treatment with conc. HCl or Lukas reagent (conc. HCl saturated with $ZnCl_2$) in dioxane.

For preparation of 19,20-dihydro analogues (compounds of formula (3) in which R^1 = Et), before or after the carbamoylation, of a compound of formula (4) or (5), a vinyl group R^1 can be reduced by hydrogenation over a palladium catalyst (*e.g.* 10% Palladium-on-carbon) in a solvent such as ethyl acetate, ethanol, dioxane, or tetrahydrofuran.

The formation of the carbamate at position 14 may be carried out as follows:

(1) Reaction of the 14-hydroxyl with an isocyanate ($R^2N=C=O$) in an inert solvent (*e.g.* CH_2Cl_2, $CHCl_3$, tetrahydrofuran, diethyl ether, dioxane), optionally in the presence of an organic or inorganic base (*e.g. N,N*-di-iso-propylethylamine, K_2CO_3). This will give an R^2NHCO_2- group at position 14. Methods for preparing isocyanate are described, for example, by J March in "Advanced Organic Chemistry", 4th ed., 1992, Wiley, New York, p.1290.

(2) Reaction of the 14-hydroxyl with an *N,N*-disubstituted carbamoyl chloride (R^2R^3NCOCl) in the presence of a hindered tertiary base (*e.g.* 2,6-lutidine, *N,N*-di-iso-propylethylamine) in an inert solvent (*e.g.* CH_2Cl_2, $CHCl_3$, tetrahydrofuran, diethyl ether, dioxane). This will give an $R^2R^3NCO_2$- group at position 14. Methods for preparing carbomoyl chlorides are described, for example, by A F Hegarty, loc. cit, p.1088.

(3) Reaction of the 14-hydroxyl with phosgene or an equivalent reagent [e.g. trichloromethyl chloroformate, bis(trichloromethyl) carbonate] in the presence of an organic base (e.g. pyridine, 2,6-lutidine, N,N-di-iso-propylethylamine), and reaction of the resulting 14-chloroformate with a primary or secondary amine (R^2NH_2 or R^2R^3NH).

Suitable hydroxy, carboxy and amino protecting groups are those well known in the art and which may be removed under conventional conditions and without disrupting the remainder of the molecule. A comprehensive discussion of the ways in which hydroxy, carboxy and amino groups may be protected and methods for cleaving the resulting protected derivatives is given in for example "Protective Groups in Organic Chemistry" (T.W. Greene, Wiley-Interscience, New York, 2nd edition, 1991). Particularly suitable hydroxy protecting groups

include, for example, triorganosilyl groups such as, for instance, trialkylsilyl and also organocarbonyl and organooxycarbonyl groups such as, for instance, acetyl, allyloxycarbonyl, 4-methoxybenzyloxycarbonyl and 4-nitrobenzyloxycarbonyl. Particularly suitable carboxy protecting groups include alkyl and aryl groups, for instance methyl, ethyl and phenyl. Particularly suitable amino protecting groups include alkoxycarbonyl, 4-methoxybenzyloxycarbonyl and 4-nitrobenzyloxycarbonyl.

In cases where the intermediate of formula (4) (such as X= acetyl) is used, a base-labile protecting group may conveniently be removed at the same time as the group X is deprotected. In cases when the intermediate of formula (5) is used, an acid-labile protecting group may conveniently be removed at the same time as the compound (5) is converted into the compound (3).

Intermediate compounds formed in the processes of this invention, for example, the 14-chloroformate derivative and the 14-*O*-carbamoyl derivatives of the compound of formula (5), are when novel also part of the invention.

The compounds of this invention may be in crystalline or non-crystalline form, and, if crystalline, may optionally be hydrated or solvated. When some of the compounds of this invention are allowed to crystallise or are recrystallised from organic solvents, solvent of crystallisation may be present in the crystalline product. This invention includes within its scope such solvates. Similarly, some of the compounds of this invention may be crystallised or recrystallised from solvents containing water. In such cases water of hydration may be present in the crystalline product. This invention includes within its scope stoichiometric hydrates as well as compounds containing variable amounts of water that may be produced by processes such as lyophilisation.

The compounds according to the invention are suitably provided in substantially pure form, for example at least 50% pure, suitable at least 60% pure, advantageously at least 75% pure, preferably at least 85% pure, more preferably at least 95% pure, especially at least 98% pure, all percentages being calculated as weight/weight. An impure or less pure form of a compound according to the invention may, for example, be used in the preparation of a more pure form of the

same compound or of a related compound (for example a corresponding derivative) suitable for pharmaceutical use.

The present invention also includes pharmaceutically acceptable salts and derivatives of the compounds of the invention. Salt formation may be possible when one of the substituents carries an acidic or basic group. Salts may be prepared by salt exchange in conventional manner.

The compounds of the present invention and their pharmaceutically acceptable salts or derivatives have antimicrobial properties and are useful for the treatment of microbial infections in animals, especially mammals, including humans, in particular humans and domesticated animals (including farm animals). The compounds may be used for the treatment of infections caused by, for example, Gram-positive and Gram-negative bacteria and mycoplasmas, including, for example, *Staphylococcus aureus, Enterococcus faecalis, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus pneumoniae, Haemophilius* sp., *Neisseria* sp., *Legionella* sp., *Mycoplasma pneumoniae, and Mycoplasma gallisepticum*.

The present invention provides a pharmaceutical composition comprising a compound of formula (3) or a pharmaceutically acceptable salt or derivative thereof together with a pharmaceutically acceptable carrier or excipient.

The present invention also provides a method of treating microbial infections in animals, especially in humans and in domesticated mammals, which comprises administering a compound of formula (3) or a pharmaceutically acceptable salt or derivative thereof, or a composition according to the invention, to a patient in need thereof.

The invention further provides the use of a compound of the invention or a pharmaceutically acceptable salt or derivative thereof in the preparation of a medicament composition for use in the treatment of microbial infections.

The compounds and compositions according to the invention may be formulated for administration in any convenient way for use in human or veterinary medicine, by analogy with other antibiotics.

The compounds and compositions according to the invention may be formulated for administration by any route, for example oral, topical or parenteral. The compositions may, for example, be made up in the form of tablets, capsules, powders, granules, lozenges, creams, syrups, or liquid preparations, for example solutions or suspensions, which may be formulated for oral use or in sterile form for parenteral administration by injection or infusion.

Tablets and capsules for oral administration may be in unit dosage form, and may contain conventional excipients including, for example, binding agents, for example, syrup, acacia, gelatin, sorbitol, tragacanth, or polyvinylpyrrollidone; fillers, for example lactose, sugar, maize-starch, calcium phosphate, sorbitol or glycine; tabletting lubricants, for example magnesium stearate, talc, polyethylene glycol or silica; disintegrants, for example potato starch; and pharmaceutically acceptable wetting agents, for example sodium lauryl sulphate. The tablets may be coated according to methods well known in normal pharmaceutical practice.

Oral liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, emulsions, syrups or elixirs, or may be presented as a dry product for reconstitution with water or another suitable vehicle before use. Such liquid preparations may contain conventional additives, including, for example, suspending agents, for example sorbitol, methyl cellulose, glucose syrup, gelatin, hydroxyethyl cellulose, carboxymethyl cellulose, aluminium stearate gel or hydrogenated edible fats; emulsifying agents, for example lecithin, sorbitan monooleate or acacia; non-aqueous vehicles (which may include edible oils), for example almond oil, oily esters (for example glycerine), propylene glycol, or ethyl alcohol; preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid; and, if desired, conventional flavouring and colour agents.

Compositions according to the invention intended for topical administration may, for example, be in the form of ointments, creams, lotions, eye ointments, eye drops, ear drops, nose drops, nasal sprays, impregnated dressings, and aerosols,

and may contain appropriate conventional additives, including, for example, preservatives, solvents to assist drug penetration, and emollients in ointments and creams. Such topical formulations may also contain compatible conventional carriers, for example cream or ointment bases, and ethanol or oleyl alcohol for lotions. Such carriers may constitute from about 1% to about 98% by weight of the formulation; more usually they will constitute up to about 80% by weight of the formulation.

Compositions according to the invention may be formulated as suppositories, which may contain conventional suppository bases, for example cocoa-butter or other glycerides.

Compositions according to the invention intended for parenteral administration may conveniently be in fluid unit dosage forms, which may be prepared utilizing the compound and a sterile vehicle, water being preferred. The compound, depending on the vehicle and concentration used, may be either suspended or dissolved in the vehicle. In preparing solutions, the compound may be dissolved in water for injection and filter-sterilised before being filled into a suitable vial or ampoule, which is then sealed. Advantageously, conventional additives including, for example, local anaesthetics, preservatives, and buffering agents can be dissolved in the vehicle. In order to enhance the stability of the solution, the composition may be frozen after being filled into the vial, and the water removed under vacuum; the resulting dry lyophilized powder may then be sealed in the vial and a accompanying vial of water for injection may be supplied to reconstitute the liquid prior to use. Parenteral suspensions may be prepared in substantially the same manner except that the compound is suspended in the vehicle instead of being dissolved and sterilisation cannot be accomplished by filtration. The compound may instead be sterilised by exposure to ethylene oxide before being suspended in the sterile vehicle. Advantageously, a surfactant or wetting agent is included in such suspensions in order to facilitate uniform distribution of the compound.

A compound or composition according to the invention may suitably be administered to the patient in an antimicrobially effective amount.

A composition according to the invention may suitably contain from 0.1% by weight, preferably from 10 to 60% by weight, of a compound according to the invention (based on the total weight of the composition), depending on the method of administration.

The compounds according to the invention may suitably be administered to the patient at a daily dosage of from 1.0 to 50 mg/kg of body weight. For an adult human (of approximately 70 kg body weight), from 50 to 3000 mg, for example about 1500 mg, of a compound according to the invention may be administered daily. Suitably, the dosage for adult humans is from 5 to 20 mg/kg per day. Higher or lower dosages may, however, be used in accordance with normal clinical practice.

When the compositions according to the invention are presented in unit dosage form, each unit dose may suitably comprise from 25 to 1000 mg, preferable from 50 to 500 mg, of a compound according to the invention.

The following Examples illustrate the present invention.

Example 1. Mutilin 14-(*N*-phenylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-phenyl-carbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (H Berner, G Schulz and H Schneider, *Tetrahedron*, 1980, 36, 1807) (170 mg) in dry CH_2Cl_2 (3 ml) was treated with phenyl isocyanate (0.12 ml) and *N,N*-di-iso-propylethylamine (1 drop) and the solution was kept at room temperature, with exclusion of moisture, for 7 days. The solution was diluted with ethyl acetate (50 ml) and was washed with dil. HCl (20 ml), water (20 ml), and saturated $NaHCO_3$ solution (20 ml). The solution was dried (Na_2SO_4) and the solvent was removed by evaporation under reduced pressure to yield a colourless oil. The oil was chromatographed on silica gel, using 1:4 ethyl acetate - hexane, to give (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-phenylcarbamate) as a colourless gum (190 mg); ν_{max} ($CHCl_3$) 3435, 1724, 1695, 1603, and 1523 cm^{-1}.

Step 2. Mutilin 14-(*N*-phenylcarbamate)

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-phenylcarbamate) (160 mg) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.2 ml) and the solution was stirred at room temperature for 3.5 hours. The mixture was diluted with ethyl acetate (50 ml) and the solution was washed with saturated NaCl solution (20 ml) and saturated $NaHCO_3$ solution (20 ml). The solution was dried (Na_2SO_4) and the solvent was removed by evaporation under reduced pressure to yield a colourless oil. The oil was chromatographed on silica gel, using 1:3 ethyl acetate - hexane, to give mutilin 14-(*N*-phenylcarbamate) as a colourless gum (145 mg); crystallisation from CH_2Cl_2 - hexane gave colourless prisms (130 mg), m.p. 211-212 °C; λ_{max} (EtOH) 236 nm (ε 19000); ν_{max} ($CHCl_3$) 3630, 3562, 3435, 1726, 1602, and 1523 cm^{-1}; MS(EI) *m/z* 439 (M^+).

Example 2. Mutilin 14-(*N*-methylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-methylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335mg, 1.0mmol) was reacted with methyl isocyanate (0.12 ml, 2.0 mmol) and *N,N* -di-iso-propyl-ethylamine (1 drop) in dichloromethane (5 ml), as for Example 1 Step 1, to afford the title compound (145 mg, 37%); ν_{max} (CH_2Cl_2) 3459, 1711, and 1516 cm^{-1}; ^1H NMR ($CDCl_3$) 6.79 (1H, dd, *J* 17.5, 10.5Hz) 5.65 (1H, d, *J* 9.9Hz) 5.31 (1H, d, *J* 10.9Hz) 5.01 (1H, d, 17.6Hz) 4.55 (1H, br) 3.46 (1H, m) 3.23 (3H, s) 2.95 (1H, q, *J* 6.4Hz) 2.83 (3H,br d, *J* 4.8Hz) 2.40 (1H, dd, *J* 15.3, 9.8Hz) 2.20 (1H, m) 2.02 (2H, m) 1.65 (3H,m) 1.47 (1H, m) 1.30-1.07 (4H, m) 1.20 (6H, s) 0.99 (3H, d, *J* 6.4Hz) 0.85 (3H, br d, *J* 6.9Hz); MS(EI) *m/z* 391 (M^+).

Step 2. Mutilin 14-(*N*-methylcarbamate)

The product of Step 1 (135 mg, 0.34 mmol) in dioxane (2ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml), as for Example 1 Step 2, to afford the title compound (89 mg, 69%); ν_{max} (CH_2Cl_2) 3460, 1732, and 1714 cm^{-1}; ^1H NMR ($CDCl_3$) 6.61 (1H, dd, *J* 17.4, 11.0Hz) 5.64 (1H, d, *J* 8.4Hz) 5.37 (1H, br d, *J* 11.0Hz) 5.21 (1H, dd, *J* 17.4, 1.6Hz) 4.47 (1H, br) 3.34 (1H, dd, *J* 11.0, 6.7Hz) 2.78 (3H, br d, *J* 4.8Hz) 2.37 (1H, quintet, *J* 6.8Hz) 2.21 (4H, m) 2.02 (2H, m) 1.70 (4H, m) 1.42 (6H, m) 1.23 (3H, s) 0.86 (3H, d, *J* 7.0Hz) 0.76 (3H, d, *J* 6Hz); MS(EI) *m/z* 377 (M^+).

Example 3. Mutilin 14-(*N-iso*-propylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N-iso*-propylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335mg, 1.0mmol) was reacted with *iso*propyl isocyanate (0.2 ml, 2.0 mmol) and *N,N* -di-iso-propyl-ethylamine (1 drop) in dichloromethane (5 ml), as for Example 1 Step 1, to afford the title compound (367 mg, 87%); ν_{max} (CH_2Cl_2) 3435, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) 6.77 (1H, dd, *J* 17.5, 10.6Hz) 5.64 (1H, d, *J* 9.8Hz) 5.30 (1H, d, *J* 10.6Hz) 5.00 (1H, d, *J* 17.5Hz) 4.44 (1H, d, *J* 7.8Hz) 3.83 (1H, m) 3.45 (1H, m) 3.22 (3H, s) 2.94 (1H, q, *J* 6.4Hz) 2.39 (1H, dd, 15.1, 9.9Hz) 2.18 (1H, m) 2.00 (2H, m) 1.65 (4H, m) 1.46 (1H, m) 1.29-1.05 (5H, m) 0.98 (3H, d, *J* 6.4Hz) 0.84 (3H, d, *J* 6.8Hz); MS(EI) *m/z* 419 (M^+).

Step 2. Mutilin 14-(*N-iso*-propylcarbamate)

The product of Step 1 (324 mg, 0.77 mmol) in dioxane (10 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml), as for Example 1 Step 2, to afford the title compound (102 mg, 33%); ν_{max} (CH_2Cl_2) 3436, 1733, 1710, 1505 cm^{-1}; ^1H NMR ($CDCl_3$) 6.60 (1H, dd, *J* 17.4, 11.0Hz) 5.64 (1H, d, *J* 8.4Hz) 5.36 (1H, dd, *J* 11.0, 1.6Hz) 5.20 (1H, dd, *J* 17.5, 1.6Hz) 4.36 (1H, br) 3.79 (1H, m) 3.34 (1H, dd, *J* 11.0, 6.6Hz) 2.38 (1H, m) 2.21 (2H, m) 2.02 (2H, m) 1.81-1.59 (4H, m) 1.49-1.26 (7H, m) 1.14 (10H, m) 0.86 (3H, d, *J* 7.1Hz) 0.76 (3H, br d, *J* 5.8Hz); MS(NH_3 DCI) *m/z* 406 (MH^+).

Example 4. Mutilin 14-(*N*-phenylsulphonylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-phenylsulphonylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) was reacted with benzenesulphonylisocyanate (0.27 ml, 2.0 mmol) and *N, N* -di-iso-propylethylamine (1 drop) in dichloromethane (5 ml), as for Example 1 Step 1, to afford the title compound (365 mg, 71%); ν_{max} (CH_2Cl_2) 3361, 1745, 1698 1450 1354cm^{-1}; ^1H NMR ($CDCl_3$) 8.05 (2H, d, *J* 7.1Hz) 7.68 (1H, t, *J* 7.3Hz) 7.57 (2H, m) 6.42 (1H, dd, *J* 17.5, 10.7Hz) 5.67 (1H, d, *J* 10.0Hz) 5.25 (1H, d, *J* 10.7Hz) 4.96 (1H, d, *J* 17.5Hz) 3.37 (1H, ddd, *J* 11.1, 8.3, 5.1Hz) 3.21 (3H, s) 2.77 (1H, q, *J* 6.4Hz) 2.32 (1H, dd, *J* 15.3, 10.0Hz) 2.16 (1H, m) 1.99 (2H, m) 1.67 (1H, d, *J* 11.3Hz) 1.48-1.02 (7H, m) 1.15 (3H, s) 1.10 (3H, s) 0.95 (3H, d, *J*

6.4Hz) 0.62 (3H, d, *J* 6.9Hz); MS(EI) *m/z* 517 (M^+), Found: 517.2504, $C_{22}H_{39}NO_6S$ requires 517.2498.

Step 2. Mutilin 14-(*N*-phenylsulphonylcarbamate)

The product of Step 1 (340 mg, 0.66 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (291 mg, 88%); mp 125-7°C; ν_{max} (CH_2Cl_2) 3364, 1736, 1450, 1420, 1353cm^{-1}; ^1H NMR ($CDCl_3$) 8.00 (2H, d, *J* 7.4Hz) 7.65 (1H, t, *J* 7.4Hz) 7.54 (2H, t, *J* 7.5Hz) 6.26 (1H, dd, *J* 17.4, 11.0Hz) 5.61 (1H, d, *J* 8.4Hz) 5.23 (1H, dd, *J* 11.0, 1.3Hz) 5.07 (1H, dd, *J* 17.5, 1.3Hz) 3.18 (1H, dd, *J* 10.1, 6.7Hz) 2.19 (3H, m) 1.95 (2H, m) 1.75-1.23 (8H, m) 1.33 (3H, s) 1.08 (1H, m) 1.07 (3H, s) 0.85 (3H, d, *J* 7.0Hz) 0.51 (3H, d, *J* 6.7Hz); MS(EI) *m/z* 503 (M^+), Found: 503.2348, $C_{27}H_{37}NO_6S$ requires 503.2342.

Example 5. Mutilin 14-(*N*-4-methoxyphenylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-4-methoxyphenylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 g, 2.97 mmol) in dry CH_2Cl_2 (10 ml) was treated with 4-methoxyphenyl isocyanate (0.77 ml, 5.95 mmol) and *N,N*-di-iso-propylethylamine (5 drops) and the solution was kept at room temperature, with exclusion of moisture, for 8 days. The solution was diluted with CH_2Cl_2 and washed with water followed by brine. The solution was dried ($MgSO_4$) and the solvent removed by evaporation under reduced pressure. The residue was triturated with ethyl acetate/hexane and the resulting solid was removed by filtration before reducing the mother liquors to low volume under reduced pressure. Purification was accomplished by chromatography on silica gel eluting with 1:4 ethyl acetate - hexane. The title compound was isolated as a foam (1.37 g, 95%); ν_{max} (CH_2Cl_2) 3428, 2932, 1722, 1697, and 1597 cm^{-1}; ^1H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.1Hz), 0.99 (3H, d, *J* 6.4Hz), 1.20 (6H, s) superimposed on 1.07-1.29 (5H, m), 1.34-1.37 (1H, m), 1.70 (1H, d, *J* 15.3Hz), 1.73 (1H, d, *J* 11.3Hz), 1.94-2.05 (2H, m), 2.15-2.24 (1H, m), 2.46 (1H, dd, *J* 15.2, 10.0Hz), 2.96 (1H, q, *J* 6.4Hz), 3.23 (3H, s), 3.47 (1H, m), 3.80 (3H, s), 5.01 (1H, d, *J* 17.4Hz), 5.31 (1H, d, *J* 10.7Hz), 5.77 (1H, d, *J* 9.9Hz), 6.43 (1H, broad s), 6.75 (1H, dd, *J* 17.5, 10.6Hz), 6.86 (2H, d, *J* 8.9Hz), 7.31 (2H, broad d); MS (ESI -ve ion) *m/z* 482 ($(M-H)^-$).

Step 2. Mutilin 14-(*N*-4-methoxyphenylcarbamate)

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-4-methoxyphenylcarbamate) (483 mg, 1mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml) as described in Example 1 Step 2. The title compound was isolated as a crystalline solid (400 mg, 86%); m.p. (CH_2Cl_2/ hexane) 192-194°C; ν_{max} (CH_2Cl_2) 3625, 3563, 2937, 1725, 1597, and 1519 cm^{-1}; ^1H NMR ($CDCl_3$) 0.79 (3H, broad d), 0.87 (3H, d, *J* 7.0Hz), 1.18 (6H, s), 1.14-1.82 (13H, m), 2.04-2.26 (3H, m), 2.37 (1H, quint, *J* 6.9Hz), 3.36 (1H, dd, *J* 10.9, 6.7Hz), 3.78 (3H, s), 4.81 (1H, dd, *J* 17.4, 1.6Hz), 5.36 (1H, dd, *J* 10.9, 1.4Hz), 5.73 (1H, d, *J* 8.3Hz), 6.39 (1H, broad s), 6.59 (1H, dd, *J* 17.4, 10.9Hz), 6.85 (2H, d, *J* 8.9Hz), 7.26 (2H, broad d); MS (EI) *m/z* 469 (M^+). $C_{28}H_{39}NO_5$ requires 469.2828, Found: 469.2830.

Example 6. Mutilin 14-(*N*-4-nitrophenylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-4-nitrophenylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0g, 2.97mmol) and 4-nitrophenyl isocyanate (731mg, 4.5mmol) and *N,N*-di-iso-propylethylamine (5 drops) were dissolved in dry CH_2Cl_2 (10ml), as described in Example 5 Step 1, to give the title compound (702mg); ν_{max} (CH_2Cl_2) 3415, 2981, 1733, 1698, and 1599 cm^{-1}; ^1H NMR ($CDCl_3$) 0.87 (3H, d, *J* 6.9Hz), 1.01 (3H, d, *J* 6.4Hz), 1.21 (3H,s) and 1.26 (3H,s) superimposed on 1.10-1.90 (6H, m), 1.68 (1H, d, *J* 15.4Hz), 1.75 (1H, d, *J* 11.5Hz), 1.94-2.06 (2H, m), 2.16-2.25 (1H, m), 2.51 (1H, dd, *J* 15.2, 10.1Hz), 2.94 (1H, q, *J* 6.3Hz), 3.23 (3H, s), 3.47-3.49 (1H, m), 5.04 (1H, d, *J* 17.5Hz), 5.32 (1H, d, *J* 10.7Hz), 5.82 (1H, d, *J* 9.9Hz), 6.70 (1H, dd, *J* 17.5, 10.6Hz), 6.93 (1H, broad s), 7.61 (2H, d, *J* 9.1Hz), 8.22 (2H, d, *J* 9.1Hz); MS (NH_3DCI) *m/z* 499 (MH^+), *m/z* 516 (MNH_4^+).

Step 2. Mutilin 14-(*N*-4-nitrophenylcarbamate)

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-4-nitrophenylcarbamate) (203 mg, 0.41 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml) as described in Example 1 Step 2. The title compound was isolated as a crystalline solid (163 mg, 82%); m.p. (CH_2Cl_2/ hexane) 208-210°C; ν_{max} (CH_2Cl_2) 3562, 3314, 2939, 1733, 1598, and 1536 cm^{-1}; ^1H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.5Hz), 0.92 (3H, d, *J* 7.0Hz), 1.20 (3H, s) and 1.46 (3H, s) both superimposed on 1.20-1.84 (10H, m),

2.09-2.28 (3H, m), 2.39 (1H, quint, *J* 7.0Hz), 3.38 (1H, dd, *J* 10.7, 6.6Hz), 5.23 (1H, dd, *J* 17.5, 1.4Hz), 5.39 (1H, dd, *J* 10.9, 1.4Hz), 5.80 (1H, d, *J* 9.3Hz), 6.56 (1H, dd, *J* 17.4, 10.9Hz), 6.88 (1H, broad s), 7.56 (2H, d, *J* 9.2Hz), 8.20 (2H, d, *J* 9.2Hz); MS (EI) *m/z* 484 (M^+). $C_{27}H_{36}N_2O_6$ requires 484.2573, Found: 484.2571.

Example 7. Mutilin 14-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-trichloroacetylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 g, 2.97 mmol) and trichloroacetyl isocyanate (0.389 ml, 3.3 mmol) and *N,N*-di-iso-propylethylamine (5 drops) were dissolved in dry CH_2Cl_2 (10 ml), as described in Example 5 Step 1, to give the title compound (1.80 g, quant.); ν_{max} (CH_2Cl_2) 3510, 3396, 1737, 1698, and 1583 cm^{-1}; ^1H NMR (d_6-acetone) 0.85-.91 (3H, m), 1.02 (3H, d, *J* 6.4Hz), 1.11-1.79 (14H, m), 1.90-2.23 (3H, m),2.42-2.63 (1H, m), 3.01 (1H, q, *J* 6.4Hz), 3.18-3.27 (5H, m), 3.50-3.59 (1H, m), 4.04-4.18 (2H, m), 4.99 (1H, d, *J* 17.6Hz), 5.30 (1H, d, *J* 10.8Hz), 5.83-5.87 (1H, m), 6.82-6.99 (m), 7.16-7,23 (m), 7.88-7.91(m) (total 4H); MS (NH_3DCI) *m/z* 521 (MH^+), *m/z* 539 (MNH_4^+).

Step 2. Mutilin 14-(*N*-trichloroacetylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-trichloroacetylcarbamate) (1.8 g, 2.97 mmol) in dioxane (10 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2.0 ml) as described in Example 1 Step 2. The title compound was isolated as a solid (901 mg, 60%); ν_{max} (CH_2Cl_2) 3406, 1803, and 1736 cm^{-1}; ^1H NMR (d_6-acetone) 0.89 (3H, d, *J* 6.8Hz), 1.01 (3H, d, *J* 6.4Hz), 1.11-2.22 (17H, m), 2.55 (1H, dd, *J* 15.4, 10.1Hz), 2.91-2.96 (1H, m), 3.19 (3H, s), 3.45-3.55 (1H, m), 5.00 (1H, d, *J* 17.6Hz), 5.31 (1H, d, *J* 10.7Hz), 5.88 (1H, d, *J* 10.0Hz), 6.74 (1H, dd, *J* 17.5, 10.7Hz), 10,59 (1H broad s); MS (ESI -ve ion) *m/z* 506 ($(M-H)^-$).

Step 3. Mutilin 14-carbamate

Mutilin 14-(*N*-trichloroacetylcarbamate) (300mg) was dissolved in CH_2Cl_2 (2 ml) and methanol (2 ml) before treating with potassium carbonate (122 mg, 0.9 mmol). The reaction was stirred at room temperature for 4 hours before diluting with CH_2Cl_2. The organic phase was washed with water (twice) followed by saturated sodium chloride solution, and the solvent removed under reduced pressure. Trituration of the residue gave the title compound as a white solid (179

mg, 85%); ν_{max} (CH_2Cl_2) 3538, 3421, 1725, and 1582 cm^{-1}; ^1H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.4Hz), 0.86 (3H, d, *J* 7.0Hz), 1.17 (3H, s), 1.39 (3H, s) superimposed on 1.38-1.79 (10H, m), 2.02-2.25 (1H, d, *J* 8.6Hz), 2.09 (1H, broad s), 2.17-2.31 (2H,m), 2.36 (1H, quint, *J* 6.9Hz), 3.35 (1H, broad t), 4.52 (2H, broad s), 5.21 (1H, dd, *J* 17.4, 1.5Hz), 5.36 (1H, dd, *J* 11.0, 1.5Hz), 5.62 (1H, d, *J* 8.5Hz) 6.57 (1H, dd, *J* 17.4, 10.9Hz); MS (NH_3DCI) *m/z* 364 (MH^+), *m/z* 381 (MNH_4^+).

Example 8. Mutilin 14-(*N*-benzylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-benzylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (336 mg, 1.0 mmol) was dissolved in dry CH_2Cl_2 (5 ml) and treated with benzyl isocyanate (0.16 ml, 1.30 mmol) and *N,N*-di-iso-propylethylamine (5 drops) and the reaction was carried out as described in Example 5, Step 1. The title compound was isolated as a white foam (432 mg, 95%); ν_{max} (CH_2Cl_2) 3444, 2930, 1711, 1698, and 1456 cm^{-1}; ^1H NMR ($CDCl_3$) 0.87 (3H, d, *J* 6.8Hz), 0.98 (3H, d, *J* 6.4Hz), 1.18 (3H, s) and 1.19 (3H, s) both superimposed on 1.02-1.54 (6H, m), 1.67 (1H, d, *J* 15.2Hz), 1.70 (1H, d, *J* 11.3Hz), 1.93-2.04 (2H, m), 2.15-2.23 (1H, m), 2.42 (1H, dd, *J* 15.1, 10.0Hz), 2.95 (1H, q, J 6.4Hz), 3.22 (3H, s), 3.42-3.51 (1H, m), 4.32 (1H, dd, *J* 14.9, 5.5Hz), 4.52 (1H, dd, *J* 14.9, 6.4Hz), 4.95 (1H, broad s), 5.01 (1H, d, *J* 17.6Hz), 5.32 (1H, d, *J* 10.7Hz), 5.69 (1H, d, *J* 9.8Hz), 6.79 (1H, dd, *J* 17.5, 10.6Hz), 7.26-7.37 (5H, m).

Step 2. Mutilin 14-(*N*-benzylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-benzylcarbamate) (400 mg, 0.85 mmol) in dioxane (5ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.0ml) as described in Example 1 Step 2. The title compound was isolated as a foam (329 mg, 82%); ν_{max} (CH_2Cl_2) 3626, 3563, 2934, 1718, 1581, and 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 0.77 (3H, d, *J* 5.9Hz), 0.86 (3H, d, *J* 7.0Hz), 1.17 (3H, s) and 1.39 (1H, s) superimposed on 1.08-1.80 (8H, m), 1.99-2.07 (3H, m), 2.17-2.24 (2H, m), 2.39 (1H, quint., *J* 6.9Hz), 3.35 (1H, dd, *J* 10.8, 6.7Hz), 4.31 (1H, dd, *J* 5.9Hz), 4.41 (1H, dd, *J* 16.0, 6.2Hz), 4.90 (1H, broad t), 5.20 (1H, d, *J* 17.3Hz), 5.36 (1H, d, *J* 10.9Hz), 5.69 (1H, d, *J* 8.4Hz), 6.61 (1H, dd, *J* 17.4, 11.0Hz), 7.24-7.43 (5H, m); MS (EI) *m/z* 391 (M^+); MS (NH_3DCI) *m/z* 392 (MH^+).

Example 9. Mutilin 14-[*N*-(Benzylaminosulfonyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(chlorosulfonyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 g, 2.97 mmol) was dissolved in dry CH_2Cl_2 (5 ml) and treated with chlorosulfonyl isocyanate (0.284 ml, 3.30 mmol) and the reaction was carried out as described in Example 5, Step 1. The title compound was isolated as a white foam (1.03 g, 75%); ν_{max} (CH_2Cl_2) 3331, 2929, 1765, 1698, and 1441 cm^{-1}; ^1H NMR ($CDCl_3$) 0.93 (3H, d, *J* 6.9Hz), 1.02 (3H, d, *J* 6.4Hz), 1.20 (3H, s) and 1.26 (3H, s) and 1.82 (1H, d, *J* 15.2Hz) all superimposed on 1.22-2.26 (5H, m), 2.60 (1H, dd, *J* 15.4, 10.2Hz), 2.95 (1H, q, *J* 6.4Hz), 2.97 (3H, s), 3.46-3.55 (1H, m), 5.02 (1H, d, *J* 17.5Hz), 5.33 (1H, d, *J* 10.7Hz), 5.88 (1H, d, *J* 10.1Hz), 6.68 (1H, dd, *J* 17.5, 10.7Hz).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(benzylaminosulfonyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(chlorosulfonyl)carbamate] (300 mg, 0.65 mmol) was dissolved in dry dichloromethane under an atmosphere of argon. The solution was treated with benzylamine (0.077 ml, 0.71 mmol) followed by triethylamine (0.1 ml, 0.71 mmol). After 12 hours stirring at room temperature the reaction was diluted with dichloromethane and washed with water and saturated sodium chloride solution. After drying ($MgSO_4$) the crude material was purified by chromatography on silica gel eluting with 1:4 ethyl acetate - hexane. The title compound was isolated as a foam (233 mg, 65%); ν_{max} (CH_2Cl_2) 3370, 2981, 2930, 1734, 1698, and 1456 cm^{-1}; ^1H NMR ($CDCl_3$) 0.88 (3H, d, *J* 6.8Hz), 0.99 (3H, d, *J* 6.4Hz), 1.19 (3H, s), 1.21 (3H, s), 1.54 (1H, d, *J* 15.4Hz), 1.72 (1H, d, *J* 11.3Hz), 1.07-1.74 (6H, m), 1.93-2.02 (2H, m), 2.14 2.23 (1H, m), 2.44 (1H, dd, *J* 15.2, 10.2Hz), 2.84 (1H, q, *J* 6.5Hz), 3.21 (3H, s), 3.38-3.47 (1H, m), 4.19 (1H, dd, *J* 13.6, 5.3Hz), 4.30 (1H, dd, *J* 13.7, 6.9Hz), 5.02 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.7Hz), 5.40 (1H, broad t, *J* ~5.7Hz) 5.74 (1H, d, *J* 10.0Hz), 6.56 (1H, dd, *J* 17.5, 10.7Hz), 7.35 (5H, broad s), 7.50 (1H, broad s); MS (NH_3DCI) *m/z* 564 (MNH_4^+); MS (EI) *m/z* 546 (M^+). $C_{29}H_{42}N_2O_6S$ requires 546.2764, Found: 546.2764.

Step 3: Mutilin 14-[*N*-(Benzylaminosulfonyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(benzylaminosulfonyl)carbamate] (233 mg, 0.43 mmol) in dioxane (4 ml) was

treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml) as described in Example 1 Step 2. The title compound was isolated as a foam (169 mg, 82%); ν_{max} (CH_2Cl_2) 3562, 3372, 2934, and 1734 cm^{-1}; ^1H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.8Hz), 0.88 (3H, d, *J* 7.0Hz), 1.20 (3H, s), 1.40 (1H, s), 1.47 (1H, d, *J* 10.7Hz), 1.10-1.81 (10H, m), 2.08-2.32 (5H, m), 3.36 (1H, dd, *J* 10.3, 6.7Hz), 4,19 (1H, s), 4.20 (1H, s), 5.26 (1H, dd, *J* 17.3, 1.4Hz), 5.37 (1H, dd, *J* 10.9, 1.3Hz), 5.34-5.39 (1H, m), 5.72 (1H, d, *J* 8.5Hz), 6.46 (1H, dd, *J* 17.4, 11.0Hz), 7.28-7.37 (5H, m); MS (NH_3DCI) *m/z* 550 (MNH_4^+).

Example 10. Mutilin 14-[*N*-(2,6-Dichloropyridin-4-yl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2,6-dichloropyridin-4-yl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (336 mg, 1.0 mmol) was dissolved in dry CH_2Cl_2 (5 ml) and treated with 2,6-dichloropyridine-4-isocyanate (283 mg, 1.5 mmol) and *N,N*-di-iso-propylethylamine (5 drops) and the reaction was carried out as described in Example 5, Step 1. The title compound was isolated as a white foam (589 mg, quant.); ν_{max} (CH_2Cl_2) 3407, 3295, 2981, 1734, 1698, 1575 and 1502 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83 (3H, d, *J* 6.9Hz), 1.01 (3H, d, *J* 6.4Hz), 1.20 (3H, s), 1.21 (3H, s), 1.08-1.56 (6H, m) 1.64 (1H, d, *J* 15.3Hz), 1.74 (1H, d, *J* 11.3Hz), 1.94-2.05 (2H, m), 2.16-2.30 (1H, m), 2.50 (1H, dd, *J* 12.7, 6.4Hz), 2.91 (1H, q, J 6.2Hz), 3.23 (3H, s), 3.41-3.48 (1H, m), 5.04 (1H, d, *J* 17.5Hz), 5.36 (1H, d, *J* 10.7Hz), 5.80 (1H, d, *J* 9.9Hz), 6.65 (1H, dd, *J* 17.6, 10.7Hz), 7.07 (1H, broad s), 7.34 (1H, s), 7.44 (1H, s); MS (NH_3DCI) *m/z* 523 (MH^+).

Step 2. Mutilin 14-[*N*-(2,6-Dichloropyridin-4-yl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2,6-dichloropyridin-4-yl)carbamate](569 mg, 1.0 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.5 ml) as described in Example 1 Step 2. The title compound was isolated as a foam which was crystallised from ethyl acetate/hexane(266 mg, 52%), m.p. (EtOAc/ hexane) 237° C; ν_{max} (CH_2Cl_2) 3404, 2926, 1739, 1719, 1579, and 1507 cm^{-1}; ^1H NMR ($CDCl_3$) 0.61 (3H, d, *J* 6.2Hz), 0.77 (3H, d, *J* 7.0Hz), 0.96-1.08 (4H, m),0.96-1.08 (10H, m), 1.90-2.27 (6H, m), 3.20-3.26 (2H, m), 5.07 (1H, dd, *J* 17.4, 1.4Hz), 5.22 (1H, dd, *J* 10.9, 1.3Hz), 5.58 (1H, d, *J* 8.3Hz), 6.34 (1H, dd, *J* 17.4, 11.0Hz), 7.34 (2H, s); MS (EI) *m/z* 508 (M^+); MS (NH_3DCI) *m/z* 509 (MH^+).

Example 11. Mutilin-14-(*N,N*-Dimethylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N,N*-dimethylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (336 mg, 1.0 mmol) was dissolved in pyridine (10 ml) before treating with *N,N*-dimethylcarbamoyl chloride (0.12 ml, 1.3 mmol). The reaction was warmed to reflux under an atmosphere of argon. Further portions of N,N-dimethylcarbamoyl chloride (0.12 ml, 1.3 mmol) were added to the reaction at 5 daily intervals during its duration. After 14 days at reflux the reaction was allowed to cool and then partitioned between ethyl acetate and 1.0*M* HCl. The organic phase was separated and washed with water followed by saturated sodium chloride solution. After drying ($MgSO_4$) the crude material was purified by chromatography on silica gel, loading in $PhCH_3$ and eluting with 1:9 ethyl acetate - hexane. The title compound was isolated as a white solid (158 mg, 40%); ν_{max} (CH_2Cl_2) 2931, 1693, and 1456 cm^{-1}; ^1H NMR ($CDCl_3$) 0.87 (3H, d, *J* 6.7Hz), 0.98 (3H, d, *J* 6.4Hz), 1.20 (3H, s) and 1.26 (3H, s) both superimposed on 1.07-1.74 (6H, m), 1.99-2.04 (2H, m), 2.16-2.24 (1H, m), 2.82 and 2.92 (3H, s+s), 2.92 (1H, m), 3.21 and 3.23 (3H, s+s), 3.46-3.56 (1H, m), 4.28 and 4.76 (ABq, *J* 15.2Hz) with 4.32 and 4.76 (ABq, *J* 15.7Hz) (total 2H), 5.01 (1H, d, *J* 17.6Hz), 5.32 (1H, d, *J* 10.2Hz), 5.72 (1H, d, *J* 9.9Hz), 6.79-6.90 (1H,m), 7.22-7.31 (5H, m).

Step 2. Mutilin-14-(*N,N*-dimethylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N,N*-dimethylcarbamate) (158 mg, 0.40 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml) as described in Example 1 Step 2. The title compound was isolated as a solid (74 mg, 49%); ν_{max} (CH_2Cl_2) 3564, 2933, 1734, 1692, and 1454 cm^{-1}; ^1H NMR ($CDCl_3$) 0.73 (3H, d, *J* 6.4Hz), 0.84 (3H, d, *J* 7.1Hz), 1.16 (3H, s) and 1.36 (1H, d, *J* 16.0Hz) and 1.45 (3H, s) all superimposed on 1.08-1.80 (5H, m), 2.00-2.10 (2H, m), 2.18-2.26 (2H, m), 2.37 (1H, quint., *J* 6.9Hz), 2.86 (3H, s), 2.90 (3H, s), 3.34 (1H, dd, *J* 11.3, 6.6Hz), 5.20 (1H, dd, *J* 17.4, 1.7Hz), 5.36 (1H, dd, *J* 11.0, 1.6Hz), 5.67 (1H, d, *J* 8.4Hz), 6.65 (1H, dd, *J* 17.4, 11.0Hz); MS (EI) *m/z* 391 (M^+); MS (NH_3DCI) *m/z* 392 (MH^+).

Example 12. 14-*O*-(Indolinylcarbonyl)mutilin

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate

Method 1

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 g, 2.97 mmol) was dissolve in dry tetrahydrofuran (10 ml) under an atmosphere of argon. The reaction was cooled to 0°C and treated with trichloromethylchloroformate (0.215 ml, 1.48 mmol) followed by triethylamine (0.495 ml, 3.56 mmol). The heterogeneous mixture was stirred at room temperature for 2 hours and then treated with further trichloromethylchloroformate (0.215 ml, 1.48 mmol) and triethylamine (0.495 ml, 3.56 mmol). After a further two hours more trichloromethylchloroformate (0.108 ml, 0.74 mmol) and triethylamine (0.250 ml, 1.78 mmol) were added. The reaction was diluted with tetrahydrofuran (30 ml) and toluene (10 ml). After washing with saturated sodium chloride the organic phase was separated and dried ($MgSO_4$). Removal of solvent gave a yellow oil which crystallised on standing (1.42 g, quant). Purification of a portion of this solid (286 mg) was accomplished by chromatography on silica gel, loading and eluting with 1:19 ethyl acetate - hexane. The title compound was isolate as a white crystalline solid (145 mg, 62%); ν_{max} (CH_2Cl_2) 1765, 1732, 1699, and 1458 cm^{-1}; ^1H NMR (d_6-acetone) 0.94 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), { 1.21 (3H, s) 1.27 (3H, s), 1.78 (1H, d, *J* 11.3Hz), 1.91 (1H, d, *J* 15.7Hz) } all superimposed on 1.11-2.26 (9H, m), 2.63 (1H, dd, *J* 15.6, 10.3Hz), 2.82 (1H, q, obscured by HOD), 3.14 (3H, s), 3.49-3.53 (1H, m), 5.02 (1H, d, *J* 17.6Hz), 5.35 (1H, d, *J* 10.7Hz), 5.83 (1H, d, *J* 10.2Hz), 6.52 (1H, dd, *J* 17.6, 10.7Hz).

Method 2

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 g, 2.97 mmol) was dissolved in toluene under an atmosphere of argon. The solution was cooled to 0°C and treated with phosgene (2.82 ml of 12.5% w/w solution in toluene, 3.56 mmol) followed by pyridine (0.24 ml, 2.97 mmol). The heterogeneous reaction mixture was stirred at room temperature. After 2 and 12 hour intervals the same quantities of phosgene and pyridine were added. The reaction mixture was then diluted with toluene (40 ml) and washed with saturated sodium chloride solution adding just enough water to completely dissolve all the solid in the aqueous phase. After drying ($MgSO_4$) the material was purified by chromatography on silica gel to give the title compound as a crystalline solid (926 mg, 78%).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-14-*O*-(indolinylcarbonyl)-4-*epi*-mutilin

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-)-4-*epi*-mutilin 14-chloroformate (300 mg, 0.75 mmol) was dissolved in dry CH_2Cl_2 whilst under an atmosphere of argon. The solution was treated with indoline (268 mg, 2.2 mmol) and the reaction stirred at room temperature for 15 minutes. The mixture was diluted with CH_2Cl_2 and washed sequentially with 1.0*M* HCl followed by water and saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and the solvents removed by evaporation under reduced pressure. Purification was achieved by chromatography on silica gel loading and eluting with 1:9 ethyl acetate - hexane. The title compound was isolated as a foam (308 mg, 86%); ν_{max} (CH_2Cl_2) 2930, 1731, 1696, and 1602 cm^{-1}; ^1H NMR (d_6-acetone) 0.85-0.91 (3H, m), 1.02 (3H, d, *J* 6.4Hz), 1.11-1.79 (14H, m), 1.90-2.23 (3H, m),2.42-2.63 (1H, m), 3.01 (1H, q, *J* 6.4Hz), 3.18-3.27 (5H, m), 3.50-3.59 (1H, m), 4.04-4.18 (2H, m), 4.99 (1H, d, *J* 17.6Hz), 5.30 (1H, d, *J* 10.8Hz), 5.83-5.87 (1H, m), 6.82-6.99 (m), 7.16-7,23 (m), 7.88-7.91(m) (total 4H); MS (EI) *m/z* 479 (M^+), (NH_3DCI) *m/z* 480 (MH^+).

Step 3: 14-*O*-(Indolinylcarbonyl)mutilin

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-14-*O*-(indolinylcarbonyl)-4-*epi*-mutilin (260 mg, 0.54 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml) as described in Example 1 Step 2. The title compound was isolated as a solid which was crystallised from CH_2Cl_2 - hexane(195 mg, 77%); ν_{max} (CH_2Cl_2) 3627. 3563, 2934, 1734, 1697, 1602, 1487, and 1407 cm^{-1}; ^1H NMR ($CDCl_3$) 0.76 (3H, m), 0.89 (3H, d, *J* 7.1Hz), 1.06-1.83 (16H, m), 2.14-2.29 (4H, m), 2.44 (1H, quint, *J* 6.9Hz), 3.12 (2H, t, *J* 8.6Hz), 3.38 (1H, m), 3.94-4.04 (1H, m), 5.22 (1H, dd, *J* 17.5, 1.5Hz), 5.38 (1H, dd, *J* 11.0, 1.5Hz), 5.72-5.86 (1H, m), 6.58-6.64 (1H, m), 6.92-6.98 (m), 7.19-7.22 (m), 7.89-7.92(m) (total 4H); MS (EI) *m/z* 465 (M^+). $C_{29}H_{39}NO_4$ requires 465.2879, Found: 465.2885.

Example 13. Mutilin 14-[*N*-(2-Hydroxyethyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2-hydroxyethyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-)-4-*epi*-mutilin 14-chloroformate (300 mg, 0.75 mmol) (prepared as described in Example 12, Step 1, Method 2)

was dissolved in dry dichloromethane (5 ml) and treated with ethanolamine (0.137 ml, 2.25 mmol) and reacted as described in Example , Step 1. The title compound was isolated as a foam (323 mg, quant.); ν_{max} (CH_2Cl_2) 3616, 3446, 2931, 1699, and 1513 cm^{-1}; ^1H NMR ($CDCl_3$) 0.85 (3H, d, *J* 6.9Hz), 0.98 (3H, d, *J* 6.4Hz), 1.23 (6H, s), 1.61 (1H, d, exchange in D_2O) superimposed on 0.95-1.72 (7H, m), 1.93-2.04 (2H, m), 2.14-2.36 (1H, m), 2.41 (1H, dd, *J* 15.2, 10.1Hz), 2.93 (1H, q, *J* 6.4Hz), 3.22 (3H, s), 3.37-3.48 (3H, m), 3.72 (2H, m, collapses to t in D_2O, *J* 5.0Hz), 5.00 (1H, d, *J* 17.6Hz) superimposed on 5.04 (1H, broad s) 5.29 (1H, d, *J* 10.8Hz), 5.69 (1H, d, *J* 9.9Hz), 6.73 (1H, dd, *J* 17.5, 10.6Hz); MS (NH_3DCI) *m/z* 422 (MH^+), *m/z* 439 (MNH_4^+).

Step 2. Mutilin 14-[*N*-(2-Hydroxyethyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2-hydroxyethyl)carbamate] (300 mg, 0.56 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml) as described in Example 1 Step 2. The title compound was isolated as a solid which was crystallised from CH_2Cl_2/ hexane(108 mg, 47%); ν_{max} (CH_2Cl_2) 3620. 3564, 3446, 2937, 1733, 1712, 1512, and 1455 cm^{-1}; ^1H NMR ($CDCl_3$) 0.76 (3H, d, *J* 6.4Hz), 0.86 (3H, d, *J* 7.0Hz), 1.08-1.81 (16H, m) {including 1.16 (3H, s), 1.40 (3H, s)}, 2.08 (1H, broad s) superimposed in 1.98-2.13 (1H, m), 2.18-2.24 (2H, m), 2.39 (1H, quint, *J* 6.9Hz), 3.31-3.38 (3H, m), 3.68 (2H, m, collapses to t in D_2O, *J* 5.0Hz), 4.98 (1H, broad t), 5.20 (1H, dd, *J* 17.5, 1.5Hz), 5.35 (1H, dd, *J* 11.3, 1.5Hz), 5.64 (1H, d, *J* 8.3Hz), 6.56 (1H, dd, *J* 17.4, 11.0Hz); MS (EI) *m/z* 484 (M^+). $C_{23}H_{37}NO_5$ requires 407.2762, Found: 407.2670.

Example 14. Mutilin 14-(*N*-Methyl-*N*-benzylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-methyl-*N*-benzylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-)-4-*epi*-mutilin 14-chloroformate (300 mg, 0.75 mmol) (prepared as described in Example 12, Step 1, Method 2) was dissolved in dry dichloromethane (5 ml) and treated with *N*-methyl-benzylamine (0.293 ml, 2.25 mmol) and reacted as described in Example , Step 1. The title compound was isolated as a foam (323 mg, 90%.); ν_{max} (CH_2Cl_2) 2981, 2929, 1698, and 1454 cm^{-1}; ^1H NMR ($CDCl_3$) 0.87 (3H, d, *J* 6.7Hz), 0.98 (3H, d, *J* 6.4Hz), 1.20 (3H, s) and 1.26 (3H, s) both superimposed on 1.07-1.74 (12H, m), 1.99-2.04 (2H, m), 2.16-2.24 (1H, m), 2.82 and 2.92 (3H, s+s), 2.92 (1H, m), 3.21 and 3.23 (3H, s+s), 3.46-3.56 (1H, m), 4.28 and 4.76 (ABq, *J*

15.2Hz) with 4.32 and 4.76 (ABq, *J* 15.7Hz) (total 2H), 5.01 (1H, d, *J* 17.6Hz), 5.32 (1H, d, *J* 10.2Hz), 5.72 (1H, d, *J* 9.9Hz), 6.79-6.90 (1H,m), 7.22-7.31 (5H, m); MS (NH_3DCI) *m/z* 482 (MH^+), *m/z* 499 (MNH_4^+); MS (EI) *m/z* 481 (M^+). $C_{30}H_{43}NO_4$ requires 481.3192, Found: 481.3199.

Step 2. Mutilin 14-(*N*-Methyl-*N*-benzylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-methyl-*N*-benzylcarbamate) (270 mg, 0.56 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml) as described in Example 1 Step 2. The title compound was isolated as a solid (187 mg, 72%); ν_{max} (CH_2Cl_2) 3656. 3564, 2932, 1734, 1688, and 1453 cm^{-1}; ^1H NMR ($CDCl_3$) 0.76 (3H, d, *J* 5.9Hz), 0.86 (3H, d, *J* 7.0Hz), 1.41-1.81 (15H, m), 1.97-2.42 (5H, m), 2.78 and 2.89 (3H, s+s), 3.32-3.38 (1H, m), 4.24 and 4.34 (1H, d+d, *J* 15.8Hz), 4.61 (1H, d, *J* 15.3Hz), 5.32 (1H, d, *J* 17.5Hz), 5.38 (1H, d, *J* 10.8Hz), 5.75 (1H, d, *J* 8.3Hz), 6.56-6.73 (1H, m), 7.20-7.31 (5H, m); MS (EI) *m/z* 467 (M^+); MS (NH_3DCI) *m/z* 468 (MH^+).

Example 15. 14-*O*-(Morpholinocarbonyl)mutilin

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-14-*O*-(morpholinocarbonyl)-4-*epi*-mutilin

Morpholine (0.2 ml, 2.29 mmol) was added to a solution of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (300 mg, 0.75 mmol) (Example 12, Step 1, Method 2) in dichloromethane (5 ml) under an atmosphere of argon. After two days the reaction was diluted with dichloromethane and washed with 1*M* HCl. The organic phase was dried ($MgSO_4$) and the solvent removed to afford the crude product. Chromatography on silica gel afforded the title compound (193 mg, 57%); ν_{max} (CH_2Cl_2) 1691cm^{-1}, ^1H NMR ($CDCl_3$) 6.79 (1H, dd, *J* 17.6, 10.7Hz), 5.86 (1H, d, *J* 9.9Hz), 5.31 (1H, d, *J* 10.7Hz), 5.01 (1H, d, *J* 17.6Hz), 3.66 (4H, m), 3.49 (5H, m), 3.22 (3H, s), 2.93 (1H, q, *J* 6.4Hz), 2.43 (1H, dd, *J* 15.2, 10.0Hz), 2.20 (1H, m), 1.99 (2H, m), 1.72 (1H, d, *J* 11.3 Hz), 1.63 (1H, d, *J* 15.2 Hz), 1.52-1.20 (5H, m), 1.23 (3H,s), 1.20 (3H, s), 1.09 (1H, m), 0.98 (3H, d, *J* 6.4Hz), 0.89 (3H, d, *J* 6.9Hz), MS(EI), *m/z* 447 (M^+) Found: 447.2990, $C_{26}H_{41}NO_5$ requires 447.2985.

Step 2. 14-*O*-(Morpholinocarbonyl)-mutilin

The product of Step 1 (153 mg, 0.34 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2,

to afford the title compound (81 mg, 55%); ν_{max} (CH_2Cl_2) 3563, 1733, and 1689 cm^{-1}, ^1H NMR ($CDCl_3$) 6.62 (1H, dd, *J* 17.4, 11.0Hz), 5.70 (1H, d, *J* 8.4Hz), 5.37 (1H, dd, *J* 11.0, 1.6Hz), 5.21 (1H, dd, *J* 17.4, 1.6Hz), 3.62 (4H, m), 3.43 (4H, m), 3.35 (1H, d, *J* 11.2, 6.6 Hz), 2.36 (1H, quintet, *J* 7.0Hz), 2.22 (2H, m), 2.10 (1H, br), 2.04 (1H, m), 1.81-1.57 (4H, m), 1.54-1.34 (4H, m), 1.43 (3H, s), 1.19 (1H, m), 1.17 (3H, s), 0.86 (3H, d, *J* 7.0Hz), 0.74 (3H, d, *J* 6.5Hz), MS(EI) *m/z* 433 (M^+) Found: 433.2834, $C_{25}H_{39}NO_5$ requires 433.2828.

Example 16. Mutilin 14-(*N*-methyl-*N*-phenylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-methyl-*N*-phenylcarbamate)

N-Methylaniline (0.3 ml, 2.32 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (300 mg, 0.75 mmol) (Example 12, Step 1, Method 2) in dichloromethane (5 ml), as for Example 12 Step 2, to afford the title compound (287 mg, 81%); ν_{max} (CH_2Cl_2) 1693 cm^{-1}; ^1H NMR ($CDCl_3$) 7.37 (2H, m), 7.24 (3H, m), 6.83 (1H, m), 5.69 (1H, m), 5.30 (1H, d, *J* 10.7Hz), 5.00 (1H, d, *J* 17.5Hz), 3.45 (1H, m), 3.32 (3H, s), 3.19 (3H, s), 2.92 (1H, m), 2.41 (1H, m), 2.18 (1H, m), 1.99 (2H, m), 1.74-1.58 (3H, m), 1.38-1.02 (11H, m), 0.97 (3H, d, *J* 6.4Hz), 0.82 (3H, m); MS(EI) *m/z* 467 (M^+) Found: 467.3040, $C_{29}H_{41}NO_4$ requires 467.3036.

Step 2. Mutilin 14-(*N*-methyl-*N*-phenylcarbamate)

The product of Step 1 (270 mg, 0.58 mmol) in dioxane (5ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (172 mg, 66%); ν_{max} (CH_2Cl_2) 3562, 1734, 1691cm^{-1}; ^1H NMR ($CDCl_3$) 7.34 (2H, m), 7.20 (3H, m), 6.64 (1H, dd, *J* 17.3, 11.0Hz), 5.71 (1H, m), 5.38 (1H, d, *J* 10.7Hz), 5.23 (1H, d, *J* 17.6Hz), 3.33 (1H, dd, *J* 11.2, 6.7Hz), 3.28 (3H, s), 2.38-2.05 (5H, m), 1.78-1.07 (9H, m), 1.58 (3H, s), 1.18 (3H, s), 0.85 (3H, d, *J* 7.0Hz), 0.74 (3H, m); MS(EI) *m/z* 453 (M^+) Found: 453.2884, $C_{28}H_{39}NO_4$ requires 453.2879.

Example 17. Mutilin 14-[*N*-(3-dimethylaminopropyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-dimethylaminopropyl)carbamate]

3-Dimethylaminopropylamine (0.07 ml, 0.56 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (170 mg, 0.43 mmol) in dichloromethane (3 ml), as for Example 12 Step2, to afford the title compound (147mg, 74%); ν_{max} (CH_2Cl_2) 3447, 1698cm^{-1}, ^{1}H NMR ($CDCl_3$) 6.78 (1H, dd, *J* 17.5, 10.7Hz), 5.62 (1H, dd, *J* 9.9Hz), 5.52 (1H, m), 5.29 (1H, d, *J* 10.7Hz), 4.99 (1H, d, *J* 17.5Hz), 3.48-3.15 (3H, m), 3.21 (3H, s), 2.94 (1H, q, *J* 6.4Hz), 2.42 (1H, m), 2.33 (2H, t, *J* 6.7Hz), 2.21 (6H, s), 2.16 (1H, m), 1.98 (2H, m), 1.83 (1H, br), 1.67 (5H, m), 1.47 (1H, m), 1.30-1.05 (3H, m), 1.18 (6H, s), 0.97 (3H, d, *J* 6.4Hz), 0.85 (3H, d, *J* 6.9Hz), MS(EI) *m/z* 462 (M^+) Found: 462.3457, $C_{27}H_{46}N_2O_4$ requires 462.3458.

Step 2. Mutilin 14-[*N*-(3-dimethylaminopropyl)carbamate]

The product of Step 1 (141 mg, 0.3 mmol) in dioxane (3 ml) was treated with concentrated HCl (1 ml), and stirred at room temperature for 24h. The reaction was carefully partitioned between ethyl acetate and saturated sodium hydrogen carbonate and the aqueous phase reextracted with ethyl acetate. The combined organics were dried ($MgSO_4$) and concentrated to afford the title compound (123mg, 90%); ν_{max} (CH_2Cl_2) 3447, 1733, 1708cm^{-1}; ^{1}H NMR ($CDCl_3$) 6.61 (1H, dd, *J* 17.4, 11.0Hz), 5.63 (1H, d, *J* 8.4Hz), 5.35 (2H, includes 1H, dd, *J* 11.0, 1.5Hz), 5.19 (1H, dd, *J* 17.4, 1.6Hz), 3.22 (3H, m), 2.35 (4H, m), 2.19 (6H, s), 2.00 (2H, m), 1.68 (7H, m), 1.42 (7H, m), 1.16 (3H, s), 1.15 (1H, m), 0.85 (3H, d, *J* 7.0Hz), 0.76 (3H, d, *J* 6.0Hz); MS(EI) *m/z* 448 (M^+) Found: 448.3302, $C_{26}H_{44}N_2O_4$ requires 448.3301.

Example 18. Mutilin 14-(*N*-hydroxycarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-hydroxycarbamate)

Hydroxylamine hydrochloride (50mg, 0.72mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (150 mg, 0.38 mmol) and di*iso*propylethylamine (0.2 ml, 1.15 mmol) in dichloromethane (3 ml), as for Example 12 Step2, to afford the title compound (80mg, 54%); ν_{max} (CH_2Cl_2) 3534, 1720, 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.18 (1H, s), 6.67 (2H includes 1H, dd, *J* 17.5, 10.6Hz), 5.73 (1H, d, *J* 9.9Hz), 5.29 (1H, d, *J* 10.7Hz),

5.02 (1H, d, 17.5Hz), 3.44 (1H, ddd, *J* 11.2, 8.0, 5.4Hz), 3.21 (3H, s), 2.89 (1H, q, *J* 6.4Hz), 2.45 (1H, dd, *J* 15.2, 10.1Hz), 2.19 (1H, m), 1.99 (2H, m), 1.72 (1H, d, *J* 11.3Hz), 1.62 (1H, d, *J* 15.2Hz), 1.49 (2H, m), 1.35-1.03 (4H, m), 1.19 (6H, s), 0.99 (3H, d, *J* 6.4Hz), 0.84 (3H, d, *J* 6.9Hz); MS(3 NOBA sodium) *m/z* 416 (MNa^+).

Step 2. Mutilin 14-(*N*-hydroxycarbamate)

The product of Step 1 (72mg, 0.18mmol) in dioxane (3ml) was treated with a saturated solution of zinc chloride in conc. HCl (1ml), as for Example 1 Step 2, to afford the title compound (47mg, 68%); ν_{max} (KBr disc) 3418, 1728cm^{-1}, ^1H NMR ($CDCl_3$) 9.38 (1H, s), 8.59 (1H, s), 6.24 (1H, dd, *J* 17.7, 11.1Hz), 5.46 (1H, d, *J* 8.0Hz), 5.11 (1H, dd, *J* 17.7, 1.8Hz), 5.04 (1H, dd, *J* 11.2, 1.9Hz), 4.46 (1H, d, *J* 6.1Hz), 3.40 (1H, m,), 2.36 (1H,br s), 2.09 (4H, m), 1.65 (2H, m), 1.49 (2H, m), 1.33 (3H, s), 1.26 (3H, m), 1.06 (4H, includes 3H, s), 0.81 (3H, d, *J* 6.8Hz), 0.67 (3H,br d, *J* 5.7Hz); MS(CI) *m/z* 397 (MNH_4^+).

Example 19. Mutilin 14-(*N*-methoxycarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-methoxycarbamate)

Methoxylamine hydrochloride (70 mg, 0.84 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (167 mg, 0.42 mmol) and di*iso*propylethylamine (0.22 ml, 1.26 mmol) in dichloromethane (3 ml), as for Example 12 Step2, to afford the title compound (164mg, 96%); ν_{max} (CH_2Cl_2) 3379, 1742, 1698 cm^{-1}, ^1H NMR ($CDCl_3$) 7.39 (1H, s), 6.70 (1H, dd, *J* 17.5, 10.7Hz), 5.73 (1H, d, *J* 10.0Hz), 5.29 (1H, d, *J* 10.7Hz), 5.00 (1H, d, 17.5Hz), 3.75 (3H,s), 3.46 (1H, ddd, *J* 11.2, 4.9, 2.9Hz), 3.21 (3H, s), 2.90 (1H, q, *J* 6.4Hz), 2.46 (1H, dd, *J* 15.3, 10.1Hz), 2.19 (1H, m), 2.00 (2H, m), 1.72 (1H, d, *J* 11.3Hz), 1.65 (1H, d, *J* 15.3Hz), 1.57 (2H, m), 1.36-1.06 (4H, m), 1.21 (3H, s), 1.19 (3H, s), 0.99 (3H, d, *J* 6.4Hz), 0.86 (3H, d, *J* 6.9Hz); MS(EI) *m/z* 407 (M^+) Found: 407.2670, $C_{23}H_{37}NO_5$ requires 407.2672.

Step 2. Mutilin 14-(*N*-methoxycarbamate)

The product of Step 1 (144 mg, 0.35 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (98mg, 70%); ν_{max} (CH_2Cl_2) 3379, 1735cm^{-1}, ^1H NMR ($CDCl_3$) 7.28 (1H, s), 6.54 (1H, dd, *J* 17.4, 11.0Hz), 5.71 (1H, d, *J* 8.5Hz), 5.37 (1H, dd, *J* 11.0, 1.5Hz), 5.22 (1H, dd, *J* 17.4, 1.5Hz), 3.71 (3H, s), 3.35 (1H,

dd, *J* 10.8, 6.7Hz), 2.34 (1H, quintet, *J* 6.9Hz), 2.23 (2H, m), 2.08 (2H, m), 1.71 (4H, m), 1.46-1.38 (4H, m), 1.42 (3H, s), 1.18 (3H, s), 1.15 (1H, m), 0.88 (3H, d, *J* 7.1Hz), 0.78 (3H, d, *J* 6.6Hz), MS(CI) *m/z* 411 (MNH_4^+), 394 (MH^+).

Example 20. Mutilin 14-(*N*-dimethylaminocarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-dimethylaminocarbamate)

1,1-Dimethylhydrazine (0.04 ml, 0.52 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (167 mg, 0.42 mmol) and di*iso*propylethylamine (0.15 ml, 0.86 mmol) in dichloromethane (3 ml), as for Example 12 Step2, to afford the title compound (130mg, 73%); ν_{max} (CH_2Cl_2) 3330, 1729, 1696 cm^{-1}, ^1H NMR ($CDCl_3$) 6.78 (1H, dd, *J* 17.5, 10.7Hz), 5.66 (1H, d, *J* 9.9Hz), 5.54 (1H, br s), 5.26 (1H, d, *J* 10.7Hz), 4.98 (1H, d, 17.5Hz), 3.46 (1H, ddd, *J* 11.2, 4.7, 2.9Hz), 3.21 (3H, s), 2.92 (1H, q, *J* 6.4Hz), 2.58 (6H,s), 2.40 (1H, dd, *J* 14.9, 10.2Hz), 2.18 (1H, m), 1.98 (2H, m), 1.64 (3H, m), 1.53-1.05 (5H, m), 1.18 (6H, s), 0.98 (3H, d, *J* 6.4Hz), 0.84 (3H, d, *J* 6.9Hz); MS(EI) *m/z* 420 (M^+) Found: 420.2994, $C_{24}H_{40}N_2O_4$ requires 420.2988.

Step 2. Mutilin 14-(*N*-dimethylaminocarbamate)

The product of Step 1 (114 mg, 0.27 mmol) in dioxane (3 ml) was treated with concentrated HCl (1ml), as for Example 17 Step 2, to afford the title compound (98mg, 89%); ν_{max} (CH_2Cl_2) 3330, 1732cm^{-1}, ^1H NMR ($CDCl_3$) 6.60 (1H, dd, *J* 17.4, 11.0Hz), 5.65 (1H, d, *J* 8.4Hz), 5.41 (1H, br s), 5.34 (1H, dd, *J* 11.0, 1.5Hz), 5.19 (1H, dd, *J* 17.4, 1.5Hz), 3.34 (1H, dd, *J* 10.9, 6.6Hz), 2.55 (6H, s), 2.36 (1H, quintet, *J* 6.9Hz), 2.22 (2H, m), 2.03 (2H, m), 1.81-1.59 (4H, m), 1.42 (7H, m), 1.16 (3H, s), 1.12 (1H, m), 0.87 (3H, d, *J* 7.0Hz), 0.76 (3H, d, *J* 6.2Hz); MS(EI) *m/z* 406 (M^+) Found: 406.2838, $C_{23}H_{38}N_2O_4$ requires 406.2832.

Example 21. Mutilin 14-[*N*-(methanesulphonylamino)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(methanesulphonylamino)carbamate]

Methanesulphonyl hydrazide (94 mg, 0.85 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (170 mg, 0.43 mmol), di*iso*propylethylamine (0.19 ml, 1.09mmol) and 4-

dimethylaminopyridine (catalytic amount) in dichloromethane (3 ml), as for Example 12 Step2, to afford the title compound (179mg, 89%); ν_{max} (CH_2Cl_2) 3372, 1716, 1698 cm^{-1}, ^1H NMR ($CDCl_3$) 6.63 (1H, dd, *J* 17.5, 10.7Hz), 5.85 (1H, d, *J* 10.1Hz), 5.31 (1H, d, *J* 10.7Hz), 5.03 (1H, d, 17.5Hz), 4.32 (2H, s), 3.47 (1H, ddd, *J* 11.3, 8.1, 5.3Hz), 3.33 (3H, s), 3.22 (3H, s), 2.87 (1H, q, *J* 6.4Hz), 2.57 (1H, dd, *J* 15.3, 10.1Hz), 2.21 (1H, m), 2.00 (2H, m), 1.76 (1H, d, *J* 11.3Hz), 1.67 (1H, d, *J* 15.3Hz), 1.54-1.05 (6H, m), 1.33 (3H, s), 1.21 (3H, s), 1.00 (3H, d, *J* 6.4Hz), 0.87 (3H, d, *J* 6.9Hz); MS(EI) *m/z* 470 (M^+).

Step 2. Mutilin 14-[*N*-(methanesulphonylamino)carbamate]

The product of Step 1 (124 mg, 0.26 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (102mg, 85%); ν_{max} (CH_2Cl_2) 3371, 1733cm^{-1}, ^1H NMR ($CDCl_3$) 6.48 (1H, dd, *J* 17.4, 11.0Hz), 5.81 (1H, d, *J* 8.6Hz), 5.37 (1H, dd, *J* 11.0, 1.4Hz), 5.23 (1H, dd, *J* 17.4, 1.4Hz), 4.28 (2H, s), 3.37 (1H, dd, *J* 10.6, 6.7Hz), 3.29 (3H, s), 2.24 (4H, m), 2.12 (1H, br s), 1.81-1.41 (8H, m), 1.59 (3H, s), 1.19 (3H, s), 1.17 (1H, m), 0.89 (3H, d, *J* 7.0Hz), 0.77 (3H, d, *J* 6.8Hz); MS(CI) *m/z* 474 (MNH_4^+).

Example 22. Mutilin 14-(*N*-methanesulphonylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-methanesulphonylcarbamate)

Methanesulphonamide (80 mg, 0.84 mmol) in DMF (0.5 ml) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (170 mg, 0.43 mmol), di*iso*propylethylamine (0.19 ml, 1.09 mmol) and 4-dimethylaminopyridine (catalytic amount) in dichloromethane (3 ml), as for Example 12 Step2, to afford the title compound (191mg, 98%); ν_{max} (CH_2Cl_2) 3364, 1742, 1698 cm^{-1}, ^1H NMR ($CDCl_3$) 6.59 (1H, dd, *J* 17.5, 10.7Hz), 5.80 (1H, d, *J* 10.0Hz), 5.31 (1H, d, *J* 10.7Hz), 5.07 (1H, d, 17.5Hz), 3.44 (1H, ddd, *J* 11.2, 8.2, 5.5Hz), 3.32 (3H, s), 3.22 (3H, s), 2.86 (1H, q, *J* 6.4Hz), 2.52 (1H, dd, *J* 15.4, 10.1Hz), 2.20 (1H, m), 1.99 (2H, m), 1.74 (1H, d, *J* 11.3Hz), 1.66 (1H, d, *J* 15.4Hz), 1.55-1.05 (6H, m), 1.23 (3H, s), 1.21 (3H, s), 1.03 (3H, d, *J* 6.4Hz), 0.88 (3H, d, *J* 6.9Hz); MS(EI) *m/z* 455 (M^+).

Step 2. Mutilin 14-(*N*-methanesulphonylcarbamate)

The product of Step 1 (144 mg, 0.32 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2,

to afford the title compound (113mg, 81%); ν_{max} (CH_2Cl_2) 3366, 1737cm^{-1}, ^{1}H NMR ($CDCl_3$) 6.45 (1H, dd, *J* 17.4, 11.0Hz), 5.75 (1H, d, *J* 8.5Hz), 5.37 (1H, dd, *J* 11.0, 1.3Hz), 5.23 (1H, dd, *J* 17.4, 1.4Hz), 3.36 (1H, dd, *J* 10.4, 6.7Hz), 3.27 (3H, s), 2.24 (4H, m), 2.09 (1H, br s), 1.81-1.40 (8H, m), 1.43 (3H, s), 1.20 (3H, s), 1.19 (1H, m), 0.89 (3H, d, *J* 7.0Hz), 0.78 (3H, d, *J* 6.8Hz); MS(CI) *m/z* 459 (MNH_4^+).

Example 23. Mutilin 14-(*N*-benzoylaminocarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-benzoylaminocarbamate)

Benzoic hydrazide(90 mg, 0.66 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (130 mg, 0.33 mmol), di*iso*propylethylamine (0.17 ml, 0.98mmol) in dichloromethane (3 ml), as for Example ? Step1, to afford the title compound (163mg, 100%); ν_{max} (CH_2Cl_2) 3403, 1729, 1696 cm^{-1}, ^{1}H NMR ($CDCl_3$) 8.12 (1H, br), 7.82 (2H, d, *J* 7.3Hz), 7.56 (1H, t, *J* 7.3Hz), 7.45 (2H, t, *J* 7.4Hz), 6.84 (1H, br), 6.68 (1H, dd, *J* 17.5, 10.7Hz), 5.73 (1H, d, *J* 9.9Hz), 5.26 (1H, d, *J* 10.7Hz), 5.00 (1H, d, 17.5Hz), 3.44 (1H, m), 3.22 (3H, s), 2.89 (1H, q, *J* 6.4Hz), 2.47 (1H, dd, *J* 15.2, 10.0Hz), 2.19 (1H, m), 2.01 (2H, m), 1.75-1.20 (13H, m), 1.12 (1H, m), 0.98 (3H, d, *J* 6.4Hz), 0.94 (3H, br d, *J* 6.5Hz); MS(EI) *m/z* 496 (M^+).

Step 2. Mutilin 14-(*N*-benzoylaminocarbamate)

The product of Step 1 (153 mg, 0.31 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (110mg, 67%); ν_{max} (CH_2Cl_2) 3405, 1734, 1691 cm^{-1}, ^{1}H NMR ($CDCl_3$) 8.14 (1H, br), 7.79 (2H, d, *J* 7.2Hz), 7.54 (1H, t, *J* 7.3Hz), 7.43 (2H, t, *J* 7.4Hz), 6.80 (1H, br), 6.52 (1H, dd, *J* 17.4, 11.1Hz), 5.69 (1H, d, *J* 8.5Hz), 5.34 (1H, dd, *J* 11.3Hz), 5.23 (1H, dd, *J* 17.4Hz), 3.36 (1H, dd, *J* 10.7, 6.5Hz), 2.27 (3H, m), 2.07 (2H, m), 1.80-1.43 (8H, m), 1.61 (3H, s), 1.19 (3H, s), 1.18 (1H, m), 0.87 (6H, d, *J* 6.9Hz); MS(EI) *m/z* 482 (M^+).

Example 24. Mutilin 14-(*N*-benzoylcarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-benzoylcarbamate)

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) was reacted with benzoyl isocyanate (0.25 ml, 2.0 mmol) in dichloromethane (5 ml), as for Example 1 Step 1, to afford the title compound (478mg, 99%); ν_{max} (CH_2Cl_2) 3423, 1777, 1714 1698 cm^{-1}, ^1H NMR ($CDCl_3$) 7.99 (1H, br s), 7.83 (2H, d, *J* 7.0Hz), 7.61 (1H, t, *J* 7.3Hz), 7.50 (2H, m), 6.73 (1H, dd, *J* 17.4, 10.6Hz), 5.85 (1H, d, *J* 9.9Hz), 5.30 (1H, d, *J* 10.7Hz), 5.02 (1H, d, 17.5Hz), 3.47 (1H, ddd, *J* 11.2, 8.3, 5.3Hz), 3.23 (3H, s), 2.91 (1H, q, *J* 6.4Hz), 2.54 (1H, dd, *J* 15.3, 10.1Hz), 2.21 (1H, m), 2.01 (2H, m), 1.75 (1H, d, *J* 11.2Hz), 1.73 (1H, d, *J* 15.3Hz), 1.62-1.08 (6H, m), 1.32 (3H, s), 1.21 (3H, s), 1.01 (3H, d, *J* 6.4Hz), 0.91 (3H, d, *J* 6.9Hz); MS(EI) *m/z* 481 (M^+) Found: 481.2823, $C_{29}H_{39}NO_5$ requires 481.2828.

Step 2. Mutilin 14-(*N*-benzoylcarbamate)

The product of Step 1 (370 mg, 0.77 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (208mg, 58%); ν_{max} (CH_2Cl_2) 3429, 1779, 1733 cm^{-1}, ^1H NMR ($CDCl_3$) 7.96 (1H, s), 7.80 (2H, d, *J* 7.1Hz), 7.59 (1H, t, *J* 7.3Hz), 7.48 (2H, t, *J* 7.4Hz), 6.56 (1H, dd, *J* 17.4, 11.0Hz), 5.84 (1H, d, *J* 8.5Hz), 5.38 (1H, dd, *J* 11.0, 1.5Hz), 5.24 (1H, dd, *J* 17.4, 1.5Hz), 3.77 (1H, dd, *J* 10.9, 6.6Hz), 2.35 (1H, quintet, *J* 7.0Hz), 2.19 (4H, m), 1.82-1.30 (8H, m), 1.52 (3H, s), 1.20 (3H, s), 1.13 (1H, m), 0.89 (3H, d, *J* 7.0Hz), 0.81 (3H, d, J = 6.6 Hz); MS(CI) *m/z* 485 (MNH_4^+).

Example 25. Antibacterial Activity

The following Table illustrates the antibacterial activities of representative 14-carbamate derivatives, in comparison with tiamulin. Activities are given as minimum inhibitory concentrations (10^{-6} g/ml), and were determined using a standard broth dilution method in microtitre.

Organism	tiamulin	mutilin 14-carbamate (Example 7)	mutilin 14-(*N*-hydroxy)carbamate (Example 18)	mutilin 14-(*N*-benzoyl)carbamate (Example 24)
B.f.	1	0.25	1	<0.06
E.c.	16	2	0.5	0.5
H.i.	2	2	1	2
M.c.	<0.06	<0.06	<0.06	<0.06
E.f.	>64	4	>64	>64
S.a.	0.25	0.5	0.5	0.125
S.e.	0.125	0.125	0.5	<0.06
S.ag.	<0.06	0.5	0.25	<0.06
S.pn.	<0.06	0.5	1	<0.06
S.p.	<0.06	0.25	1	<0.06

B.f. = *Bacteroides fragilis* B70; E.c. = *Escherichia coli* DC2; H.i. = *Haemophilus influenzae* Q1; M.c. = *Moraxella catarrhalis* 1502; E.f. = *Enterococcus faecalis* 1; S.a. = *Staphylococcus aureus* Oxford;

S.e. = *Staphylococcus epidermidis* PHLN 20; S. ag. = *Streptococcus agalactiae* Hester; S. pn. = *Streptococcus pneumoniae* 1761; S.p. = *Streptococcus pyogenes* CN 10.

Example 26. Mutilin 14-[*N*-(2-phenylethyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2-phenylethyl)carbamate]

Phenethylamine (0.16 ml, 1.29 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (170 mg, 0.43 mmol) in dichloromethane (5 ml), as described in Example 12, Step 2, to afford the title compound (200 mg, 97%); ν_{max} (CH_2Cl_2) 2902, 2254, 1794, 1703, 1644, and 1465 cm^{-1}; ^1H NMR ($CDCl_3$) 0.84 (3H, d, *J* 6.9Hz), 0.97 (3H, d, *J* 6.4Hz), 1.05-2.27 (12H, m) including 1.14 (3H, s) and 1.18 (3H, s), 2.38 (1H, dd, *J* 15.3, 10.0Hz), 2.82 (1H, dd, *J* 13.2, 6.9Hz), 2.94 (1H, q, *J* 6.4Hz), 3.21 (3H, s), 3.37-3.61 (3H, m), 4.65 (1H, broad t), 5.00 (1H, d, *J* 17.5Hz), 5.31 (1H, d, *J* 10.6Hz), 5.64 (1H, d, *J* 9.8Hz), 6.75 (1H, dd, *J* 17.8, 10.7Hz), 7.18-7.34 (5H, m); MS (NH_3DCI) *m/z* 482 (MH^+).

Step 2. Mutilin 14-[*N*-(2-phenylethyl)carbamate]

The product of Step 1 (200 mg, 0.42 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml), as for Example 1, Step

2, to afford the title compound (75 mg, 39%); ν_{max} (CH_2Cl_2) 3445, 1733, 1712, and 1635 cm^{-1}; ^1H NMR ($CDCl_3$) 0.75 (3H, broad s), 0.86 (3H, d, *J* 7.0Hz), 1.06-2.23 (18H, m) including 1.16 (3H, s) and 1.35 (3H, s), 2.37 (1H, quint., *J* 6.6Hz), 2.77 (1H, q, *J* 6.5Hz), 3.30-3.51 (3H, m), 4.11 (2H, q, *J* 7.2Hz), 4.66 (1H, broad s), 5.21 (1H, dd, *J* 17.3, 1.2Hz), 5.35 (1H, d, *J* 10.8Hz), 5.64 (1H, d, *J* 8.3Hz), 6.58 (1H, dd, *J* 17.4, 10.9Hz), 7.14-7.31 (5H, m); MS(EI) *m/z* 467 (M^+), MS (NH_3DCI) *m/z* 468 (MH^+).

Example 27. Mutilin 14-[*N*-(1-(R)-phenyl-2-hydroxy)ethylcarbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-(R)-phenyl-2-hydroxy)ethylcarbamate]

(R)-2-Phenylglycinol (177 mg, 1.29 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (170 mg, 0.43 mmol) in dichloromethane (5 ml), as described in Example 12, Step 2, to afford the title compound (220 mg, quant.); ν_{max} (CH_2Cl_2) 3600, 3433, 2931, 1698, and 1503 cm^{-1}, ^1H NMR ($CDCl_3$) 0.82 (3H, d, *J* 6.6Hz), 0.95 (3H, d, *J* 6.4Hz), 0.98-2.22 (18H, m), 2.43 (1H, dd, *J* 15.3, 10.0Hz), 2.87 (1H, q, *J* 6.5Hz), 3.23 (3H, s), 3.46 (1H, s), 3.89 (2H, m), 4.13 (2H, dd, *J* 14.3, 7.1Hz), 4.87 (1H, broad s), 4.99 (1H, d, *J* 17.5Hz), 5.27 (1H, d, *J* 7.3Hz), 5.64 (1H, d, *J* 9.9Hz), 6.66 (1H, dd, *J* 17.4, 10.6Hz), 7.27-7.37 (5H, m).

Step 2. Mutilin 14-[*N*-(1-(R)-phenyl-2-hydroxy)ethylcarbamate]

The product of Step 1 (212 mg, 0.42 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml), as for Example 1 Step 2, to afford the title compound (81 mg, 39%); ν_{max} (CH_2Cl_2) 3565, 3433, 2961, 1732, 1713, and 1503 cm^{-1}; ^1H NMR ($CDCl_3$) 0.73 (3H, broad d), 0.84 (3H, d, *J* 7.0Hz), 0.97-1.76 (18H, m), 1.93-2.30 (3H, m), 2.32 (1H, quint., *J* 6.6Hz), 3.25-3.40 (1H, m), 3.70-3.95 (2H, m), 4.75-4.87 (1H, broad s), 5.15-5.35 (3H, m), 5.62 (1H, d, *J* 8.3Hz), 7.27-7.37 (5H,m); MS(EI) *m/z* 483 (M^+), (NH_3DCI) *m/z* 484 (MH^+).

Example 28. Mutilin 14-[*N*-2-(methoxycarbonyl)ethylcarbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-2-(methoxycarbonyl)ethylcarbamate]

β-Alanine methyl ester hydrochloride (120 mg, 0.86 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (170 mg, 0.43 mmol) and N,N-di*iso*propylethylamine (0.150 ml, 0.86 mmol) in dichloromethane (5 ml), as described in Example 12, Step 2, to afford the title compound (185 mg, 93%); ν_{max} (CH_2Cl_2) 3446, 2930, 1733, 1709, 1509, and 1456 cm^{-1}; ^1H NMR ($CDCl_3$) 0.81 (3H, d, *J* 6.9Hz), 0.97 (3H, d, *J* 6.4Hz), 1.04-1.71 (14H, m), 1.92-2.04 (2H, m), 2.13-2.22 (1H, m), 2.39 (1H, dd, *J* 15.2, 10.0Hz), 2.55 (2H, t, *J* 5.7Hz), 2.92 (1H, q, *J* 6.4Hz), 3.21 (3H, s), 3.41-3.54 (3H, m), 3.69 (3H, s), 4.99 (1H, d, *J* 17.6Hz), 5.13 (1H, t, *J* 6.0Hz), 5.28 (1H, d, *J* 10.7Hz), 5.63 (1H, d, *J* 9.9Hz), 6.74 (1H, dd, *J* 17.5, 10.7Hz); MS (NH_3DCI) *m/z* 464 (MH^+), *m/z* 481 (MNH_4^+)

Step 2. Mutilin 14-[*N*-2-(methoxycarbonyl)ethylcarbamate]

The product of Step 1 (200 mg, 0.42 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml) and the reaction stirred at room temperature overnight. The solution was poured into ethyl acetate and saturated sodium chloride solution. The aqueous phase was reextracted with ethyl acetate and the combined organic phases were washed with saturated sodium hydrogen carbonate solution (twice). The organic phase was finally washed with saturated sodium chloride solution and dried ($MgSO_4$). Purification was accomplished by chromatography on silica gel, loading in dichloromethane and eluting with mixtures of ethyl acetate in hexane. The title compound was isolated as a foam (21 mg, 12%); ν_{max} (CH_2Cl_2) 3564, 3446, 1734, 1713, and 1509 cm^{-1}; ^1H NMR ($CDCl_3$) 0.71 (3H, broad d, *J* 6.0Hz), 0.85 (3H, d, *J* 7.0Hz), 1.07-1.79 (15H, m) including 1.13 (3H, s) and 1.37 (3H, s), 1.96-2.23 (4H, m), 2.35 (1H, quint., *J* 6.9Hz), 2.52 (2H, t, *J* 5.9Hz), 3.30-3.50 (3H, m), 3.67 (3H, s), 5.06 (1H, broad t), 5.26 (1H, dd, *J* 17.5, 1.5Hz), 5.34 (1H, dd, *J* 11.0, 1.5Hz), 5.62 (1H, d, *J* 8.4Hz), 6.56 (1H, dd, *J* 17.4, 11.0Hz); MS(EI) *m/z* 449 (M^+), (NH_3DCI) *m/z* 450 (MH^+).

Example 29. Mutilin 14-[*N*-2-carboxyethylcarbamate]

Step 1. Mutilin 14-[*N*-2-carboxyethylcarbamate]

The sodium hydrogen carbonate solutions from Example 28, Step 2, were acidified with hydrchloric acid (5M) and the resulting solution extracted with ethyl acetate (twice). After washing the organic phase with saturated sodium chloride solution it was dried ($MgSO_4$) and the solvent removed by evaporation *in vacuo* to give the title compound as a white solid (43 mg, 24%); ν_{max} (CH_2Cl_2) 3446, 2961, 1730, 1714, and 1509 cm^{-1}; ^1H NMR ($CDCl_3$) 0.72 (3H, broad d, *J* 5.7Hz), 0.86 (3H, d, *J* 7.0Hz), 0.97-1.79 (15H, m), 1.96-2.23 (5H, m), 2.55-2.60 (2H, m), 3.34-3.46 (3H, m), 5.07-5.38 (3H, m), 5.61-5.68 (1H, m), 6.50-6.52 (1H, m); MS(EI) *m/z* 435 (M^+); MS (NH_3DCI) *m/z* 436 (MH^+), *m/z* 453 (MNH_4^+).

Example 30. Mutilin 14-[*N*-(hydroxyiminobenzyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(hydroxyiminobenzyl)carbamate]

Benzamidoxime (129 mg, 0.94 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (170 mg, 0.43 mmol) in dichloromethane (3 ml), as described in Example 12, Step 2, to afford the title compound (180 mg, 84%); ν_{max} (CH_2Cl_2) 3519, 3414, 2930, 1759, 1697, 1640, 1586, and 1457 cm^{-1}; ^1H NMR ($CDCl_3$) 0.93 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.60 (13H, m) including 1.20 (3H, s) and 1.30 (3H, s), 1.74 (1H, d, *J* 11.2Hz), 1.77 (1H, d, *J* 15.3Hz), 1.94-2.04 (2H, m), 2.15-2.24 (1H, m), 2.52 (1H, dd, *J* 15.2, 10.2Hz), 2.88 (1H, q, *J* 6.4Hz), 3.23 (3H, s), 3.43-3.54 (1H, m), 4.99 (1H, d, *J* 17.4Hz), 5.09 (1H, broad s), 5.27 (1H, d, *J* 10.8Hz), 5.70 (1H, d, *J* 10.0Hz), 6.75 (1H, dd, *J* 17.5, 10.7Hz), 7.38-7.52 (3H, m), 7.69-7.73 (2H, m); MS (NH_3DCI) *m/z* 497 (MH^+).

Step 2. Mutilin 14-[*N*-(hydroxyiminobenzyl)carbamate]

The product of Step 1 (160 mg, 0.33 mmol) in dioxane (4 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.8 ml), as for Example 1, Step 2, to afford the title compound (114 mg, 72%); ν_{max} (CH_2Cl_2) 3520, 3414, 2932, 1761, 1733, 1710, 1640, and 1587 cm^{-1}; ^1H NMR ($CDCl_3$) 0.84 (3H, d, *J* 6.7Hz), 0.88 (3H, d, *J* 7.1Hz), 0.99-1.82 (16H, m) including 1.19 (3H, s) and 1.50 (3H, s), 2.08-2.34 (4H, m) including 2.32 (1H, quint., *J* 6.8Hz), 3.36 (1H, dd, *J* 10.5, 6.6Hz), 5.06 (2H, broad s), 5.23 (1H, dd, *J* 17.3, 1.5Hz), 5.37 (1H, dd,

J 11.2, 1.4Hz), 5.69 (1H, d, *J* 8.6Hz), 6.57 (1H, dd, *J* 17.3, 11.0Hz), 7.26-7.51 (3H, m), 7.67-7.71 (2H, m); MS (NH_3DCI) *m/z* 483 (MH^+).

Example 31. Mutilin 14-[*N*-(4-methoxybenzoyl)carbamate]

Step 1. 4-Methoxybenzoylisocyanate

Silver cyanate (689 mg, 4.6 mmol) was suspended in dry dichloromethane (5 ml) under an atmosphere of argon. A solution of 4-methoxybenzoylchloride (682 mg, 4.0 mmol) in dichloromethane (5 ml) was added and the heterogeneous mixture stirred at reflux under subdued light according to the method of Arcus *et. al.* (*J. Chem. Soc.* **1954**, 4018). After one hour the reaction was allowed to cool and filtered through Kieselguhr. The solution was used immediately in the next reaction. ν_{max} (CH_2Cl_2) 2246 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-methoxybenzoyl)carbamate]

The solution from step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 1 hour. The mixture was diluted with dichloromethane and washed with 1.0M hydrochloric acid followed by water and saturated sodium chloride solution. After drying ($MgSO_4$) the crude material was purified by chromatography on silica gel, loading in dichloromethane and eluting with 20% ethyl acetate in hexane. Evaporation of solvents *in vacuo* gave the title compound (488 mg, 95%); m.p. (CH_2Cl_2/ hexane) 168°C; ν_{max} (CH_2Cl_2) 3427, 3300, 2931, 1774, 1697, 1605, and 1479cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.56 (12H, m) including 1.20 (3H, s) and 1.32 (3H, s), 1.72 (1H, d, *J* 15.3Hz), 1.74 (1H, d, *J* 11.2Hz), 1.94-2.04 (2H, m), 2.16-2.24 (1H, m), 2.53 (1H, dd, *J* 15.2, 10.1Hz), 2.91 (1H, q, *J* 6.2Hz), 3.23 (3H, s), 3.42-3.50 (1H, m), 3.87 (3H, s), 5.00 (1H, d, *J* 17.5Hz), 5.29 (1H, d, *J* 10.7Hz), 5.84 (1H, d, *J* 9.9Hz), 6.73 (1H, dd, *J* 17.4, 10.6Hz), 6.97 (2H, d, *J* 8.9Hz), 7.81 (2H, d, *J* 8.9Hz); MS (EI) *m/z* 511 (MH^+); (NH_3DCI) *m/z* 512 (MH^+); (Found: C, 70.38; H, 8.21; N, 2.91. $C_{30}H_{41}NO_6$ requires C, 70.42; H, 8.08; N, 2.74)

Step 3. Mutilin 14-[*N*-(4-methoxybenzoyl)carbamate]

The product of Step 2 (440 mg, 0.85 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (140 mg, 33%); m.p. (CH_2Cl_2/ hexane) 108°C

(dec.); ν_{max} (CH_2Cl_2) 3564, 3429, 2961, 1776, 1733, 1710, 1607, and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.81 (3H, d, *J* 6.6Hz), 0.88 (3H, d, *J* 7.0Hz), 1.10-1.81 (15H, m) including 1.15 (3H, s) and 1.51 (3H, s), 2.12 (1H, bs) superimposed on 2.09-2.26 (2H, m), 2.35 (1H, quint., *J* 6.9Hz), 3.36 (1H, dd, *J* 11.0, 6.6Hz), 3.86 (3H, s), 5.22 (1H, dd, *J* 17.3, 1.5Hz), 5.37 (1H, dd, *J* 11.0, 1.4Hz), 5.83 (1H, d, *J* 8.5Hz), 6.56 (1H, dd, *J* 17.3, 11.0Hz), 6.95 (2H, d, *J* 8.8Hz), 7.77 (2H, d, *J* 8.8Hz), 7.88 (1H, bs); MS (NH_3DCI) *m/z* 498 (MH^+); (Found: C, 69.88; H, 7.67; N, 2.93. $C_{29}H_{39}NO_6$ requires C, 70.00; H, 7.90; N, 2.81)

Example 32. Mutilin 14-[*N*-(4-nitrobenzoyl)carbamate]

Step 1. 4-Nitrobenzoylisocyanate

Silver cyanate (689 mg, 4.6 mmol) was suspended in dry dichloromethane (5 ml) under an atmosphere of argon. A solution of 4-nitrobenzoylchloride (682 mg, 4.0 mmol) in dichloromethane (5 ml) was added and the reaction treated as described in Example 31, Step 1. The solution was used immediately in the next reaction.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-nitrobenzoyl)carbamate]

The solution from Step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 1 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (480 mg, 91%); ν_{max} (CH_2Cl_2) 3406, 2959, 1780, 1733, 1698, 1607, and 1531cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 1.03 (3H, d, *J* 6.4Hz), 1.08-1.59 (12H, m) including 1.20 (3H, s) and 1.31 (3H, s), 1.69 (1H, d, *J* 15.5Hz), 1.75 (1H, d, *J* 11.6Hz), 1.93-2.05 (2H, m), 2.15-2.25 (1H, m), 2.54 (1H, dd, *J* 15.2, 10.1Hz), 2.89 (1H, q, *J* 6.4Hz), 3.22 (3H, s), 3.41-3.50 (1H, m), 5.01 (1H, d, *J* 17.5Hz), 5.28 (1H, d, *J* 10.7Hz), 5.84 (1H, d, *J* 9.9Hz), 6.64 (1H, dd, *J* 17.4, 10.7Hz), 8.00 (2H, d, *J* 8.7Hz), 8.22 (1H, bs), 8.35 (2H, d, *J* 8.9Hz); MS (NH_3DCI) *m/z* 544 (MNH_4^+).

Step 3. Mutilin 14-[*N*-(4-nitrobenzoyl)carbamate]

The product of Step 2 (440 mg, 0.83 mmol) in dioxane (10 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (282 mg, 66%); ν_{max} (CH_2Cl_2) 3551, 3412, 2959, 1786, 1734, 1699, 1607, and 1531cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.8Hz), 0.88 (3H, d, *J* 7.0Hz), 1.10-1.23 (4H, m), 1.41-1.82 (12H, m) including 1.50 (3H, s), 2.11 (1H, bs), 2.14-2.34 (3H, m), 3.37 (1H, dd, *J* 10.7, 6.6Hz), 5.24

(1H, dd, *J* 17.3, 1.4Hz), 5.36 (1H, dd, *J* 10.9, 1.3Hz), 5.81 (1H, d, *J* 8.5Hz), 6.49 (1H, dd, *J* 17.3, 11.0Hz), 7.94 (2H, d, *J* 8.8Hz), 8.04 (1H, bs), 8.33 (2H, d, *J* 8.8Hz).

Example 33. Mutilin 14-[*N*-(3-nitrobenzoyl)carbamate]

Step 1. 3-Nitrobenzoylisocyanate

Silver cyanate (689 mg, 4.6 mmol) was suspended in dry dichloroethane (5 ml) under an atmosphere of argon. A solution of 3-nitrobenzoylchloride (682 mg, 4.0 mmol) in dichloroethane (5 ml) was added and the reaction stirred at reflux for 4 hours before treating as described in Example 31, Step 1. The solution was used immediately in the next reaction. ν_{max} (CH_2Cl_2) 2247cm^{-1}

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-nitrobenzoyl)carbamate]

The solution from Step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 1 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (523 mg, quant.); ν_{max} (CH_2Cl_2) 3406, 2930, 1781, 1720, 1698, 1618, and 1537cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.91 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), 1.08-1.60 (12H, m) including 1.20 (3H, s) and 1.30 (3H, s), 1.67-1.77 (2H, m), 2.00-2.05 (2H, m), 2.15-2.25 (1H, m), 2.55 (1H, dd, *J* 15.3, 10.1Hz), 2.89 (1H, q, *J* 6.3Hz), 3.22 (3H, s), 3.41-3.50 (1H, m), 5.01 (1H, d, *J* 17.5Hz), 5.24 (1H, d, *J* 10.7Hz), 5.86 (1H, d, *J* 10.0Hz), 6.62 (1H, dd, *J* 17.4, 10.6Hz), 7.73 (1H, t, *J* 8.0Hz), 8.20 (1H, d, *J* 7.9Hz), 8.23 (1H, s), 8.46 (1H, dd, *J* 7.8, 1.0Hz), 8.67 (1H, m); MS (NH_3DCI) *m/z* 544 (MNH_4^+).

Step 3. Mutilin 14-[*N*-(3-nitrobenzoyl)carbamate]

The product of Step 2 (483 mg, 0.92 mmol) in dioxane (10 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (280 mg, 66%); m.p. (CH_2Cl_2/ hexane) 121°C; ν_{max} (CH_2Cl_2) 3564, 3418, 2940, 1782, 1733, 1617, and 1537cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.7Hz), 0.88 (3H, d, *J* 6.9Hz), 1.09-1.23 (4H, m), 1.40-1.81 (12H, m), 2.11 (1H, bs), 2.14-2.33 (3H, m), 3.36 (1H, dd, *J* 10.7, 6.7Hz), 5.23 (1H, dd, *J* 17.4, 1.4Hz), 5.31 (1H, dd, *J* 10.9, 1.2Hz), 5.81 (1H, d, *J* 8.0Hz), 6.49 (1H, dd, *J* 17.3, 11.0Hz), 7.71 (1H, t, *J* 8.0Hz), 8.17 (1H, dt, *J* 7.9, 1.3Hz), 8.29 (1H, bs), 8.43 (1H, dt, *J* 8.0, 1.1Hz), 8.64 (1H, t, *J* 1.9Hz); MS (NH_3DCI)

m/z 530 (MNH_4^+); (Found: C, 65.95; H, 7.23; N, 5.35. $C_{28}H_{36}N_2O_7$ requires C, 65.61; H, 7.08; N, 5.46).

Example 34. Mutilin 14-[*N*-(4-aminobenzoyl)carbamate]

Mutilin 14-[*N*-(4-nitrobenzoyl)carbamate] (79 mg, 0.15 mmol) was suspended in ethanol (10 ml). Addition of ethyl acetate (2 ml) brought about complete dissolution. Tin (II) chloride (146 mg, 0.75 mmol) was added and the reaction warmed to reflux whilst under an atmosphere of argon. After an hour the reaction was allowed to cool and poured into ethyl acetate/ water before neutralising with sodium hydrogen carbonate. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane. The title compound was isolated as a coloured foam (44 mg, 61%); ν_{max} (CH_2Cl_2) 3684, 3405, 2933, 1782, 1773, 1733, 1605, and 1473cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.5Hz), 0.88 (3H, d, *J* 7.0Hz), 1.09-1.26 (4H, m), 1.40-1.81 (12H, m), 2.04-2.37 (4H, m), 3.36 (1H, dd, *J* 10.6, 6.6Hz), 4.13 (2H, bs), 5.22 (1H, dd, *J* 17.4, 1.5Hz), 5.36 (1H, dd, *J* 11.0, 1.3Hz), 5.78 (1H, d, *J* 8.4Hz), 6.56 (1H, dd, *J* 17.4, 11.0Hz), 6.65 (2H, d, *J* 8.7Hz), 7.64 (2H, d, *J* 8.7Hz), 7.83 (1H, bs); MS (NH_3DCI) *m/z* 483 (MH^+).

Example 35. Mutilin 14-[*N*-(3-aminobenzoyl)carbamate]

Mutilin 14-[*N*-(3-nitrobenzoyl)carbamate] (100 mg, 0.19 mmol) was suspended in ethanol (10 ml). Addition of ethyl acetate (2 ml) brought about complete dissolution. Tin (II) chloride (185 mg, 1.0 mmol) was added and the reaction treated as described in Example 34. The title compound was isolated as a coloured foam (55 mg, 60%); ν_{max} (CH_2Cl_2) 3395, 2932, 1778, 1733, 1716, 1624, and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.88 (3H, d, *J* 7.0Hz), 1.10-1.82 (16H, m, including 1.19 (3H, s) and 1.51 (3H, s)), 2.09-2.37 (4H, m), 3.37 (1H, dd, *J* 10.8, 6.6Hz), 3.86 (2H, bs), 5.23 (1H, dd, *J* 17.4, 1.5Hz), 5.39 (1H, dd, *J* 11.0, 1.4Hz), 5.82 (1H, d, *J* 8.5Hz), 6.58 (1H, dd, *J* 17.3, 11.0Hz), 6.86 (1H, dd, *J* 7.8, 2.4Hz), 7.06 (1H, d, *J* 7.8Hz), 7.13 (1H, t, *J* 2.0Hz), 7.23 (1H, t, *J* 7.8Hz), 7.88 (1H, bs); MS (ESI, -ve ion) *m/z* 481 ($M-H^-$).

Example 36. Mutilin 14-[*N*-(2-hydroxybenzoyl)carbamate]

Step 1. 2-Acetoxybenzoylisocyanate

Silver cyanate (689 mg, 4.6 mmol) and O-acetylsalicoyl chloride (794 mg, 4.0 mmol) in dichloroethane (10 ml) were reacted in the manner described in Example 33, Step 1. The title compound was immediately used in the next reaction.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2-acetoxybenzoyl)carbamate]

The solution from Step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 1 hour. The title compound (80% pure) was isolated by the same procedure as described in Example 31, Step 2 (385 mg, 70 %); ν_{max} (CH_2Cl_2) 3411, 2981, 2931, 1778, 1732, 1698, 1606, and 1480cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), 1.08-1.60 (12H, m) including 1.20 (3H, s) and 1.26 (3H, s), 1.67-1.76 (2H, m), 1.95-2.05 (2H, m), 2.15-2.25 (1H, m), 2.38 (3H, s), 2.50 (1H, dd, *J* 15.3, 10.1Hz), 2.88 (1H, q, *J* 6.3Hz), 3.22 (3H, s), 3.42-3.48 (1H, m), 5.00 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.7Hz), 5.81 (1H, d, *J* 10.0Hz), 6.72 (1H, dd, *J* 17.4, 10.6Hz), 7.21-7.42 (2H, m), 7.68 (1H, dt, *J* 7.8, 1.4Hz), 8.09 (1H, dd, *J* 7.9, 1.6Hz), 8.36 (1H, bs), 8.46 (1H, dd, *J* 7.8, 1.0Hz), 8.67 (1H, m); MS (EI) *m/z* 539 (MH^+); (NH_3DCI) *m/z* 540 (MH^+).

Step 3. Mutilin 14-[*N*-(3-hydroxybenzoyl)carbamate]

The product of Step 2 (385 mg, 0.50 mmol of 80% pure material) in dioxane (10 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2. The crude material was dissolved in ethanol (2 ml) and treated with 1.0M sodium hydroxide for 1 hour at room temperature. The solution was poured into ethyl acetate in hexane and water. The organic phase was washed with saturated sodium chloride and dried ($MgSO_4$). Purification was accomplished by chromatography on silica gel eluting with 10% acetone in toluene. The title compound was isolated as a white solid (115 mg, 47%); m.p. (CH_2Cl_2/ hexane) 170°C; ν_{max} (CH_2Cl_2) 3566, 3434, 2960, 1775, 1733, 1673, and 1493cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 6.9Hz), 1.09-1.25 (4H, m), 1.37-1.81 (12H, m), 2.11-2.33 (4H, m), 3.37 (1H, dd, *J* 10.2, 6.6Hz), 5.22 (1H, dd, *J* 17.4, 1.3Hz), 5.35 (1H, dd, *J* 10.9, 1.1Hz), 5.81 (1H, d, *J* 8.5Hz), 6.52 (1H, dd, *J* 17.3, 11.0Hz), 6.90 (1H, td, *J* 7.5, 0.8Hz), 7.02 (1H, dd, *J*

8.3, 0.9Hz), 7.18-7.28 (1H, m), 7.95 (1H, d, *J* 7.6Hz), 8.45 (1H, bs), 11.31 (1H, bs); MS (ESI -ve ion) *m/z* 482 ($M-H^-$).

Example 37. Mutilin 14-[*N*-(4-Acetoxybenzoyl)carbamate]

Step 1. 4-Acetoxybenzoylisocyanate

Silver cyanate (950 mg, 6.3 mmol) and 4-acetoxybenzoyl chloride (1.09 g, 5.5 mmol) in dichloroethane (10 ml) were reacted in the manner described in Example 34, Step 1. The title compound was immediately used in the next reaction; ν_{max} (CH_2Cl_2) 2240 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-acetoxybenzoyl)carbamate]

The solution from Step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (446 mg, 1.27 mmol) and the reaction stirred for 1 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (620 mg, 91%); ν_{max} (CH_2Cl_2) 3420, 2930, 1777, 1762, 1731, 1714, 1698, 1604, and 1478cm^{-1}; ^1H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.56 (12H, m), 1.72 (1H, d, *J* 15.4Hz), 1.74 (1H, d, *J* 11.2Hz), 1.94-2.10 (2H, m), 2.15-2.48 (1H, m), 2.33 (3H, s), 2.53 (1H, dd, *J* 15.2, 10.0Hz), 2.90 (1H, q, *J* 6.4Hz), 3.22 (3H, s), 3.42-3.50 (1H, m), 5.02 (1H, d, *J* 17.5Hz), 5.29 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 9.9Hz), 6.72 (1H, dd, *J* 17.5, 10.7Hz), 7.24 (2H, d, *J* 8.7Hz), 7.86 (2H, d, *J* 8.7Hz), 8.02 (1H, bs).

Step 3. Mutilin 14-[*N*-(4-acetoxybenzoyl)carbamate]

The product of Step 2 (570 mg, 1.05 mmol) in dioxane (10 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (56 mg, 11%); ν_{max} (CH_2Cl_2) 3563, 3419, 2960, 1778, 1761, 1733, 1718, 1604, and 1479cm^{-1}; ^1H NMR ($CDCl_3$) 0.40 (3H, d, *J* 6.6Hz), 0.88 (3H, d, *J* 7.0Hz), 1.10-1.28 (4H, m), 1.38-1.82 (13H, m), 2.12-2.37 (6H, m), 3.37 (1H, dd, *J* 10.8, 6.6Hz), 5.24 (1H, dd, *J* 17.3, 1.4Hz), 5.38 (1H, dd, *J* 11.1, 1.4Hz), 5.83 (1H, d, *J* 8.7Hz), 6.56 (1H, dd, *J* 17.4, 11.0Hz), 7.22 (2H, d, *J* 8.7Hz),, 7.83 (2H, d, *J* 8.7Hz), 8.22 (1H, bs); MS (FAB, NOBA/Na) *m/z* 548 (MNa^+).

Example 38. Mutilin 14-[*N*-(4-hydroxybenzoyl)carbamate]

The title compound was isolated from the reaction described in Example 37, Step 3 (134 mg, 27%); ν_{max} (KBr disc) 1764, 1730, and 1690; ^{1}H NMR ($CDCl_3$ + CD_3OD) 0.76 (3H, d, *J* 6.4Hz), 0.84 (3H, d, *J* 6.9Hz), 1.05-1.21 (4H, m), 1.37-1.78 (11H, m), 2.00-2.34 (4H, m), 3.32 (1H, d, *J* 6.5Hz), 5.19 (1H, dd, *J* 17.4, 1.4Hz), 5.32 (1H, d, *J* 11.0Hz), 5.77 (1H, d, *J* 8.7Hz), 6.51 (1H, dd, *J* 17.4, 11.0Hz), 6.82 (2H, d, *J* 8.7Hz),, 7.66 (2H, d, *J* 8.7Hz); MS (FAB, NOBA/Na) *m/z* 506 (MH^+) *m/z* 548 (MNa^+).

Example 39. Mutilin 14-[*N*-(3-methoxybenzoyl)carbamate]

Step 1. 3-Methoxybenzoylisocyanate

Silver cyanate (689 mg, 4.6 mmol) and 3-methoxybenzoylchloride (563 ul, 4.0 mmol) in dry dichloromethane (10 ml) were reacted according to the method described in Example 31, Step 1. The solution containing the title compound was immediately used in the next reaction.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-methoxybenzoyl)carbamate]

The solution from Step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (336 mg, 1.00 mmol) and the reaction stirred for 1 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (430 mg, 84%); m.p. (CH_2Cl_2/ hexane) 110-112°C; ν_{max} (CH_2Cl_2) 3419, 2931, 1770, 1714, 1697, 1601, and 1585cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.56 (12H, m) including 1.20 (3H, s) and 1.32 (3H, s), 1.72 (1H, d, *J* 15.4Hz), 1.75 (1H, d, *J* 11.3Hz), 1.94-2.06 (2H, m), 2.16-2.25 (1H, m), 2.53 (1H, dd, *J* 15.2, 10.1Hz), 2.90 (1H, q, *J* 6.5Hz), 3.23 (3H, s), 3.42-3.50 (1H, m), 3.86 (3H, s), 5.01 (1H, d, *J* 17.4Hz), 5.30 (1H, d, *J* 10.8Hz), 5.85 (1H, d, *J* 9.9Hz), 6.73 (1H, dd, *J* 17.5, 10.7Hz), 7.13 (1H, ddd, *J* 6.8, 2.6, 1.0Hz), 7.31-7.43 (3H, m), 7.99 (1H, bs); MS (NH_3DCI) *m/z* 512 (MH^+); (Found: C, 70.38; H, 8.28; N, 2.91. $C_{30}H_{41}NO_6$ requires C, 70.42; H, 8.08; N, 2.74)

Step 3. Mutilin 14-[*N*-(3-methoxybenzoyl)carbamate]

The product of Step 2 (440 mg, 0.85 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (170 mg, 45%); m.p. (CH_2Cl_2/ hexane) 117°C

(dec.); ν_{max} (CH_2Cl_2) 3556, 3423, 2961, 1779, 1733, and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.88 (3H, d, *J* 6.9Hz), 1.10-1.81 (16H, m) including 1.23 (3H, s) and 1.52 (3H, s), 2.04-2.37 (4H, m), 3.36 (1H, dd, *J* 10.9, 6.5Hz), 3.85 (3H, s), 5.23 (1H, dd, *J* 17.3, 1.5Hz), 5.37 (1H, dd, *J* 10.9, 1.4Hz), 5.83 (1H, d, *J* 8.5Hz), 6.56 (1H, dd, *J* 17.3, 10.9Hz), 7.11 (1H, ddd, *J* 8.0, 2.4, 1.3Hz), 7.28-7.41 (3H, m), 7.98 (1H, bs); MS (NH_3DCI) *m/z* 498 (MH^+), *m/z* 515 (MNH_4^+).

Example 40. Mutilin 14-[*N*-(2-methoxybenzoyl)carbamate]

Step 1. 2-Methoxybenzoylisocyanate

Silver cyanate (689 mg, 4.6 mmol) and 3-methoxybenzoylchloride (593 ul, 4.0 mmol) in dry dichloromethane (10 ml) were reacted according to the method described in Example 31, Step 1. The solution containing the title compound was immediately used in the next reaction: ν_{max} (CH_2Cl_2) 2250 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2-methoxybenzoyl)carbamate]

The solution from Step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (336 mg, 1.00 mmol) and the reaction stirred for 1 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (500 mg, 98%); ν_{max} (CH_2Cl_2) 3344, 2981, 2931, 1772, 1732, 1698, 1602, and 1509cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 1.01 (3H, d, *J* 6.4Hz), 1.07-1.59 (12H, m) including 1.20 (3H, s) and 1.33 (3H, s), 1.75 (1H, d, *J* 11.2Hz), 1.77 (1H, d, *J* 15.4Hz), 1.95-2.04 (2H, m), 2.16-2.25 (1H, m), 2.50 (1H, dd, *J* 15.2, 10.1Hz), 2.91 (1H, q, *J* 6.3Hz), 3.23 (3H, s), 3.44-3.51 (1H, m), 4.04 (3H, s), 5.00 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.7Hz), 5.78 (1H, d, *J* 9.9Hz), 6.82 (1H, dd, *J* 17.5, 10.7Hz), 7.02 (1H, d, *J* 8.0Hz), 7.10 (1H, td, *J* 7.5, 0.7Hz), 7.54 (1H, td, *J* 7.8, 1.8Hz), 8.24 (1H, dd, *J* 7.8, 1.8Hz), 10.00 (1H, bs); MS (ESI, -ve ion) *m/z* 510 ($M-H^-$).

Step 3. Mutilin 14-[*N*-(2-methoxybenzoyl)carbamate]

The product of Step 2 (430 mg, 0.83 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (208 mg, 49%); m.p. (CH_2Cl_2/ hexane) 142-145°C; ν_{max} (CH_2Cl_2) 3626, 3563, 3346, 2953, 1773, 1733, 1701 and 1609cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.81 (3H, d, *J* 6.6Hz), 0.88 (3H, d, *J* 7.0Hz), 1.15-1.81 (16H, m) including 1.22 (3H, s) and 1.52 (3H, s), 2.04-2.38 (4H, m), 3.36 (1H, dd, *J* 11.1,

6.5Hz), 4.01 (3H, s), 5.23 (1H, dd, *J* 17.3, 1.5Hz), 5.39 (1H, dd, *J* 10.9, 1.4Hz), 5.78 (1H, d, *J* 8.5Hz), 6.62 (1H, dd, *J* 17.4, 11.0Hz), 7.11 (1H, t, *J* 7.6Hz), 7.52 (1H, td, *J* 7.8, 1.8Hz), 8.20 (1H, dd, *J* 7.8, 1.8Hz), 9.89 (1H, bs); MS (ESI, +ve ion) *m/z* 520 (MNa^+).

Example 41. Mutilin 14-[*N*-(phenylacetyl)carbamate]

Step 1. Phenylacetylisocyanate

Silver cyanate (689 mg, 4.6 mmol) and phenylacetylchloride (0.563 ml, 4.0 mmol) in dry dichloromethane (10 ml) were reacted according to the method described in Example 31, Step 1. The solution containing the title compound was immediately used in the next reaction.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(phenylacetyl)carbamate]

The solution from Step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (336 mg, 1.00 mmol) and the reaction stirred for 1 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (500 mg, quant.); m.p. (CH_2Cl_2/ hexane) 187-8 °C; ν_{max} (CH_2Cl_2) 3383, 2930, 1784, 1751, 1698, and 1479cm^{-1}; ^1H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.00-1.61 (13H, m), 1.72 (1H, d, *J* 11.3Hz), 1.92-2.05 (2H, m), 2.14-2.23 (1H, m), 2.46 (1H, dd, *J* 15.3, 10.1Hz), 2.88 (1H, q, *J* 6.5Hz), 3.21 (3H, s), 3.38-3.48 (1H, m), 4.10 (2H, s), 5.03 (1H, d, *J* 17.4Hz), 5.32 (1H, d, *J* 10.7Hz), 5.72 (1H, d, *J* 9.9Hz), 6.63 (1H, dd, *J* 17.5, 10.7Hz), 7.24-7.38 (5H, m), 7.50 (1H, bs); MS (NH_3DCI) *m/z* 496 (MH^+), *m/z* 513 (MNH_4^+).

Step 3. Mutilin 14-[*N*-(phenylacetyl)carbamate]

The product of Step 2 (460 mg, 0.93 mmol) in dioxane (10 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (202 mg, 45%); m.p. (CH_2Cl_2/ hexane) 187°C; ν_{max} (CH_2Cl_2) 3564, 3386, 2941, 1784, 1752, 1733, and 1477cm^{-1}; ^1H NMR ($CDCl_3$) 0.68 (3H, d, *J* 6.7Hz), 0.89 (3H. d, *J* 7.0Hz), 1.09-1.82 (15H, m) including 1.22 (3H, s) and 1.40 (3H, s), 2.00-2.38 (5H, m), 3.36 (1H, dd, *J* 10.4, 6.7Hz), 4.02 and 4.12 (2H, ABq, *J* 15.7Hz), 5.23 (1H, dd, *J* 17.5, 1.4Hz), 5.38 (1H, dd, *J* 10.9, 1.3Hz), 5.71 (1H, d, *J* 8.4Hz), 6.57 (1H, dd, *J* 17.3, 11.1Hz), 7.24-7.35 (5H, m), 7.51 (1H, bs); MS (NH_3DCI) *m/z* 482 (MH^+), *m/z* 499 (MNH_4^+).

Example 42. Mutilin 14-[*N*-(4-carboxybenzoyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-formylbenzoyl)carbamate]

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (680 mg, 2.00 mmol) was combined with 4-formylbenzoyl chloride (1.68g, 10.0 mmol), silver cyanate (1.50 g, 10.0 mmol) and tetrakis(triphenylphosphine) palladium (0) (25 mg) in dry dichloromethane (25 ml) and the reaction stirred at room temperature for 6 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with 1.0M hydrochloric acid followed by water and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel, loading in dichloromethane and eluting with mixtures of ethyl acetate in hexane. The title compound was isolated as a crystalline solid (700 mg, 70%); ν_{max} (CH_2Cl_2) 3406, 2930, 1778, 1707, 1576, and 1480cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), 1.04-1.62 (12H, m), 1.73-1.77 (2H, m), 1.94-2.24 (2H, m), 2.15-2.25 (1H, m), 2.54 (1H, dd, *J* 15.2, 10.0Hz), 2.88 (1H, q, *J* 6.3Hz), 3.22 (3H, s), 3.41-3.48 (1H, m), 5.02 (1H, d, *J* 17.5Hz), 5.28 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 10.0Hz), 6.67 (1H, dd, *J* 17.5, 10.0Hz), 7.95-8.03 (5H, m), 8.13 (1H, bs), 10.11 (1H, s); MS (NH_3DCI) *m/z* 527 (MNH_4^+). (Found: C, 70.46; H, 8.03; N, 2.55. $C_{30}H_{39}NO_6$ requires C, 70.70; H, 7.71; N, 2.75).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-carboxybenzoyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-formylbenzoyl)carbamate] (200 mg, 0.4 mmol) was dissolved in acetone (5 ml) and treated with Jones' reagent (0.05 ml of 8M solution of [O], 0.4 mmol) and the reaction was stirred at room temperature for 5 minutes. More Jones' reagent (0.05 ml) was added and stirring continued at room temperature. The reaction mixture was treated with isopropanol (1 ml) and then partitioned between ethyl acetate and water. After washing the organic phase with water and brine it was dried ($MgSO_4$). Removal of solvent *in vacuo* gave the title compound as a foam (182mg, 87%); ν_{max} (CH_2Cl_2) 3434, 3273, 2927, 17323, and 1699cm^{-1}; ^{1}H NMR ($CDCl_3$, CD_3OD)) 0.84 (3H, d, *J* 6.8Hz), 0.93 (3H, d, *J* 6.3Hz), 1.01-1.54 (13H, m), 1.62-1.69 (2H, m), 2.08-2.17 (2H, m), 2.44 (1H, dd, *J* 15.2, 10.0Hz), 2.85 (1H, q, *J* 6.3Hz), 3.16 (3H, s), 3.36-3.41 (1H, m), 4.94 (1H, d, *J* 17.4Hz), 5.23 (1H, d, *J* 10.8Hz), 5.78 (1H, d, *J* 9.8Hz), 6.65 (1H, dd, *J* 17.5, 10.7Hz), 7.84 (2H, d, *J* 8.5Hz), 8.05 (2H, d, *J* 8.5Hz); MS (NH_3DCI) *m/z* 543 (MNH_4^+).

Step 3. Mutilin 14-[*N*-(4-carboxybenzoyl)carbamate]

The product of Step 2 (600 mg, 1.14 mmol) in dioxane (15 ml) was treated with a saturated solution of zinc chloride in conc. HCl (3.5 ml), as for Example 1 Step 2, to afford the title compound (280 mg, 68%); ν_{max} (KBr disc) 1766, 1740, and 1709cm^{-1}; ^{1}H NMR (d_6-Acetone) 0.82 (3H, d, *J* 6.3Hz), 0.96 (3H, d, *J* 7.0Hz), 1.19-1.25 (4H, m), 1.39-1.84 (10H, m), 2.07-2.36 (5H, m), 3.36 (1H, bs, collapse to d in D_2O, *J* 6.0Hz), 5.19 (1H, dd, *J* 11.2, 1.8Hz), 5.27 (1H, dd, *J* 17.7, 1.6Hz), 5.79 (1H, d, *J* 8.5Hz), 6.45 (1H, dd, *J* 17.6, 11.2Hz), 8.01 (1H, d, *J* 8.5Hz), 8.14 (1H, d, *J* 8.1Hz), 10.04 (1H, s, ex. in D_2O); MS (ESI, +ve ion) *m/z* 534 (MNa^+).

Example 43. Mutilin 14-(*N*-phenoxycarbamate)

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-phenoxycarbamate)

O-Phenylhydroxylamine hydrochloride (165 mg, 1.13 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (150 mg, 0.38 mmol) and di*iso*propylethylamine (0.33 ml, 1.9 mmol) in dichloromethane (3 ml), as for Example 12 Step2, to afford the crude title compound (150mg) which was used in the following step without purification; ν_{max} (CH_2Cl_2) 3368, 1753, 1698 cm^{-1}; ^{1}H NMR *inter alia*($CDCl_3$) 0.87 (3H, d, *J* 6.9Hz), 0.98 (3H, d, *J* 6.4Hz) 1.13 (3H, s), 1.20 (3H, s), 1.05-1.30 (4H, m), 1.52 (2H, m), 1.69 (1H, d, *J* 15.4Hz), 1.71 (1H, d, *J* 11.2Hz), 1.98 (2H, m), 2.18 (1H, m), 2.48 (1H, dd, *J* 15.3, 10.1Hz), 2.88 (1H, q, *J* 6.4Hz), 3.20 (3H, s), 3.44 (1H, m), 5.01 (1H, d, 17.5Hz), 5.28 (1H, d, *J* 10.6Hz), 5.76 (1H, d, *J* 10.0Hz), 6.69 (1H, dd, *J* 17.4, 10.6Hz), 7.08 (3H, m), 7.31 (2H, m), 7.63 (1H, s); MS(CI) *m/z* 487 (MNH_4^+).

Step 2. Mutilin 14-(*N*-phenoxycarbamate)

The product of Step 1 (112 mg) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (11.5 mg); ν_{max} (CH_2Cl_2) 3562, 1735cm^{-1}, ^{1}H NMR ($CDCl_3$) 0.68 (3H,br), 0.86 (3H, d, *J* 6.9Hz), 1.06-1.79 (9H, m), 1.16 (3H, s), 1.29 (3H, s), 2.05 (2H, m), 2.23 (3H, m), 3.33 (1H, m,), 5.21 (1H, dd, *J* 17.2, 1.3Hz), 5.36 (1H, d, *J* 11.1Hz), 5.75 (1H, d, *J* 8.3Hz), 6.46 (1H, dd, *J* 17.3, 11.0Hz), 6.91 (1H, d, *J* 7.9Hz), 7.06 (1H, t, *J* 7.3Hz), 7.28 (2H, m); MS(EI) *m/z* 456 (M^+) Found: 455.2677, $C_{27}H_{37}NO_5$ requires 455.2672.

Example 44. Mutilin 14-[*N*-(4-trifluoromethylbenzoyl)carbamate]

Step 1. 4-Trifluoromethylbenzoylisocyanate

Silver cyanate (690 mg, 4.6 mmol) and 4-trifluoromethylbenzoylchloride (0.6 ml, 4.0 mmol) in dry dichloromethane (5 ml) were reacted according to the method described in Example 31, Step 1. The solution containing the title compound was immediately used in the next reaction; ν_{max} (CH_2Cl_2) 2246 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-trifluoromethylbenzoyl)carbamate]

The solution from step 1 was treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.00 mmol) and the reaction stirred for 1.5 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (405 mg, 74%); ν_{max} (CH_2Cl_2) 3416, 1780, 1718, 1698cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.85 (1H, m), 0.90 (3H, d, *J* 6.9Hz), 1.01 (3H, d, *J* 6.4Hz), 1.08-1.31 (3H, m), 1.21 (3H, s), 1.31 (3H, s), 1.52 (2H, m), 1.74 (2H, m), 2.03 (2H, m), 2.21 (1H, m), 2.54 (1H, dd, *J* 15.2, 10.1Hz), 2.89 (1H, q, *J* 6.4Hz), 3.23 (3H, s), 3.46 (1H, m), 5.02 (1H, d, *J* 17.4Hz), 5.30 (1H, d, *J* 10.6Hz), 5.85 (1H, d, *J* 10.0Hz), 6.68 (1H, dd, *J* 17.4, 10.6Hz), 7.77 (1H, d, *J* 8.3Hz), 7.94 (1H, d, *J* 8.2Hz), 8.02 (1H, s); MS (EI) *m/z* 549 (M^+) Found: 549.2703, $C_{30}H_{38}F_3NO_5$ requires 549.2702.

Step 3. Mutilin 14-[*N*-(4-trifluoromethylbenzoyl)carbamate]

The product of Step 2 (385 mg, 0.7 mmol) in dioxane (6 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (148 mg, 40%); ν_{max} (CH_2Cl_2) 3421, 1781, 1734cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 7.0Hz), 1.18 (1H, m) 1.20 (3H, s) 1.51 (3H, s), 1.41-1.82 (8H, m), 2.04-2.36 (5H, m), 3.37 (1H, dd, *J* 10.7, 6.6Hz), 5.24 (1H, dd, *J* 17.4, 1.4Hz), 5.37 (1H, dd, *J* 11.0, 1.3Hz), 5.82 (1H, d, *J* 8.5Hz), 6.53 (1H, dd, *J* 17.3, 11.0Hz), 7.75 (2H, d, *J* 8.3Hz), 7.90 (1H, d, *J* 8.2Hz), 7.98 (1H, bs); MS (CI) *m/z* 553 (MNH_4^+).

Example 45. Mutilin 14-[*N*-(3-trifluoromethylbenzoyl)carbamate]

Step 1. 3-Trifluoromethylbenzoylisocyanate

Silver cyanate (690 mg, 4.6 mmol) and 3-trifluoromethylbenzoylchloride (0.6 ml, 3.98 mmol) in dry dichloromethane (5 ml) were reacted according to the method described in Example 31, Step 1. The solution containing the title compound was immediately used in the next reaction; ν_{max} (CH_2Cl_2) 2250 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-trifluoromethylbenzoyl)carbamate]

The solution from step 1 was treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 1.5 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (480 mg, 87%); ν_{max} (CH_2Cl_2) 3414, 1780, 1718, 1698cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), 1.05-1.43 (4H, m), 1.21 (3H, s), 1.30 (3H, s), 1.53 (2H, m), 1.71 (1H, d, *J* 15.3Hz), 1.75 (1H, d, *J* 11.2Hz), 2.00 (2H, m), 2.20 (1H, m), 2.55 (1H, dd, *J* 15.2, 10.1Hz), 2.89 (1H, q, *J* 6.4Hz), 3.22 (3H, s), 3.46 (1H, ddd, *J* 11.2, 5.3, 2.9Hz), 5.02 (1H, d, *J* 17.5Hz), 5.28 (1H, d, *J* 10.7Hz), 5.86 (1H, d, *J* 10.0Hz), 6.67 (1H, dd, *J* 17.5, 10.7Hz), 7.65 (1H, t, *J* 7.8Hz), 7.86 (1H, d, *J* 7.9Hz), 8.01 (1H, d, *J* 7.9Hz), 8.09 (2H, brs); MS (CI) *m/z* 567 (MNH_4^+) (Found: C, 65.50; H, 6.90; N, 2.71. $C_{30}H_{38}F_3NO_5$ requires C, 65.56; H, 6.97; N, 2.55).

Step 3. Mutilin 14-[*N*-(3-trifluoromethylbenzoyl)carbamate]

The product of Step 2 (350 mg, 0.64 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (184 mg, 54%); ν_{max} (CH_2Cl_2) 3411, 1781, 1734cm^{-1}; ^1H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 6.9Hz), 1.15 (1H, m) 1.20 (3H, s) 1.51 (3H, s), 1.41-1.81 (8H, m), 2.11-2.35 (5H, m), 3.37 (1H, dd, *J* 10.9, 6.6Hz), 5.23 (1H, dd, *J* 17.3, 1.4Hz), 5.35 (1H, dd, *J* 11.0, 1.3Hz), 5.82 (1H, d, *J* 8.5Hz), 6.52 (1H, dd, *J* 17.3, 11.0Hz), 7.63 (1H, t, *J* 7.8Hz), 7.84 (1H, d, *J* 7.8Hz), 7.98 (1H, d, *J* 7.8Hz) 8.06 (1H, s), 8.12 (1H, s); MS (Electrospray) *m/z* 558 (MNa^+).

Example 46. Mutilin 14-[*N*-(2-trifluoromethylbenzoyl)carbamate]

Step 1. 2-Trifluoromethylbenzoylisocyanate

Silver cyanate (690 mg, 4.6 mmol) and 2-trifluoromethylbenzoylchloride (0.5 ml, 3.4 mmol) in dry dichloromethane (5 ml) were reacted according to the method described in Example 31, Step 1 for 3 hours. The solution containing the title compound was immediately used in the next reaction; ν_{max} (CH_2Cl_2) 2254 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2-trifluoromethylbenzoyl)carbamate]

The solution from step 1 was treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 0.5 hour. The title compound was isolated by the same procedure as described in Example 31, Step 2 (231 mg, 42%): ν_{max} (CH_2Cl_2) 3384, 1782, 1760, 1698cm^{-1}; ^1H NMR ($CDCl_3$) 0.85 (3H, d, *J* 6.8Hz), 0.95 (3H, d, *J* 6.4Hz), 1.05-1.36 (4H, m), 1.19 (6H, s), 1.50 (2H, m), 1.62 (1H, d, *J* 15.4Hz), 1.71 (1H, d, *J* 11.3Hz), 1.98 (2H, m), 2.17 (1H, m), 2.48 (1H, dd, *J* 15.3, 10.1Hz), 2.81 (1H, q, *J* 6.4Hz), 3.21 (3H, s), 3.43 (1H, m), 4.98 (1H, d, *J* 17.5Hz), 5.23 (1H, d, *J* 10.7Hz), 5.72 (1H, d, *J* 10.0Hz), 6.50 (1H, dd, *J* 17.4, 10.6Hz), 7.50 (1H, m,), 7.64 (2H, m), 7.76 (2H, m); MS (CI) *m/z* 567 (MNH_4^+).

Step 3. Mutilin 14-[*N*-(2-trifluoromethylbenzoyl)carbamate]

The product of Step 2 (207 mg, 0.38 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (149 mg, 74%); ν_{max} (CH_2Cl_2) 3390, 1784, 1763, 1734, 1705cm^{-1}; ^1H NMR ($CDCl_3$) 0.76 (3H, d, *J* 6.9Hz), 0.83 (3H, d, *J* 7.0Hz), 1.16 (1H, m) 1.18 (3H, s) 1.38 (3H, s), 1.36-1.49 (4H, m),1.55-1.76 (4H, m), 2.04-2.28 (5H, m), 3.33 (1H, dd, *J* 10.6, 6.7Hz), 5.19 (1H, dd, *J* 17.3, 1.3Hz), 5.28 (1H, d, *J* 11.0Hz), 5.67 (1H, d, *J* 8.4Hz), 6.36 (1H, dd, *J* 17.2, 11.0Hz), 7.44 (1H, m), 7.62 (2H, m), 7.72 (2H, m); MS (CI) *m/z* 553 (MNH_4^+).

Example 47. Mutilin 14-[*N-iso*-nicotinoylcarbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N-iso*-nicotinoylcarbamate]

A mixture of silver cyanate (690 mg, 4.6 mmol), *iso*-nicotinoyl chloride hydrochloride (535 mg, 3.0 mmol), *tetrakis* tripheylphosphine palladium (0) (18.5 mg, 0.016 mmol) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) in dichloromethane (15 ml) was protected from light and stirred at room temperature under argon for 66 hour. Di*iso*propylethylamine (1 ml) was then added and the reaction mixture filtered through Kieselguhr. Concentration afforded a crude product which was purified by silica gel chromatography eluting with 50-75% ethyl acetate/hexane mixtures to give the title compound (212 mg, 44%); ν_{max} (CH_2Cl_2) 3406, 1781, 1721, 1698cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.9Hz), 1.01 (3H, d, *J* 6.4Hz), 1.03-1.62 (6H, m), 1.21 (3H, s), 1.31 (3H, s), 1.70 (1H, d, *J* 15.5Hz), 1.75 (1H, d, *J* 11.5Hz), 2.00 (2H, m), 2.21 (1H, m), 2.54 (1H, dd, *J* 15.2, 10.1Hz), 2.88 (1H, q, *J* 6.3Hz), 3.22 (3H, s), 3.46 (1H, ddd, *J* 11.2, 8.3, 5.3Hz), 5.02 (1H, d, *J* 17.5Hz), 5.29 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 10.0Hz), 6.66 (1H, dd, *J* 17.5, 10.7Hz), 7.64 (2H, dd, *J* 4.4, 1.6Hz), 8.11 (1H, s), 8.84 (2H, dd, *J* 4.4, 1.5Hz); MS (CI) *m/z* 483 (MNH_4^+).

Step 2. Mutilin 14-[*N-iso*-nicotinoylcarbamate]

The product of Step 1 (177 mg, 0.37 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (29.6 mg, 17%); ν_{max} (CH_2Cl_2) 3400, 1783, 1734cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.8Hz), 0.89 (3H, d, *J* 7.0Hz), 1.16 (1H, m) 1.20 (3H, s) 1.50 (3H, s), 1.44-1.82 (8H, m), 2.11-2.35 (5H, m), 3.37 (1H, dd, *J* 10.7, 6.6Hz), 5.23 (1H, dd, *J* 17.3, 1.4Hz), 5.36 (1H, dd, *J* 10.9, 1.3Hz), 5.82 (1H, d, *J* 8.5Hz), 6.51 (1H, dd, *J* 17.3, 11.0Hz), 7.62 (1H, dd, *J* 4.5, 1.5Hz), 8.20 (1H, s), 8.79 (2H, dd, *J* 4.5, 1.7Hz); MS (CI) *m/z* 469 (MH^+).

Example 48. Mutilin 14-[*N*-nicotinoylcarbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-nicotinoylcarbamate]

A mixture of silver cyanate (690 mg, 4.6 mmol), nicotinoyl chloride hydrochloride (712 mg, 4.0 mmol), *tetrakis* tripheylphosphine palladium (0) (14 mg, 0.012 mmol), di*iso*propylethylamine (0.7 ml, 4.0 mmol) and (3*R*)-3-deoxo-

11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) in dichloromethane (14 ml) was protected from light and stirred at reflux under argon for 50 minutes. The reaction mixture was filtered through Kieselguhr and concentrated, to afforded a crude product which was purified by silica gel chromatography to give the title compound (177 mg, 37%); ν_{max} (CH_2Cl_2) 3410, 1779, 1717, 1698cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), 1.08-1.56 (6H, m), 1.21 (3H, s), 1.30 (3H, s), 1.71 (1H, d, *J* 15.3Hz), 1.75 (1H, d, *J* 11.2Hz), 2.00 (2H, m), 2.21 (1H, m), 2.54 (1H, dd, *J* 15.3, 10.1Hz), 2.89 (1H, q, *J* 6.4Hz), 3.22 (3H, s), 3.46 (1H, ddd, *J* 11.2, 8.1, 5.4Hz), 5.02 (1H, d, *J* 17.4Hz), 5.28 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 10.0Hz), 6.67 (1H, dd, *J* 17.5, 10.7Hz), 7.46 (1H, dd, *J* 7.6, 4.9Hz), 8.16 (2H, m), 8.81 (1H, dd, *J* 4.9, 1.5Hz) 9.02 (1H, d, *J* 2.3Hz); MS (CI) *m/z* 483 (MNH_4^+).

Step 2. Mutilin 14-[*N*-nicotinoylcarbamate]

The product of Step 1 (153 mg, 0.32 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (95 mg, 64%); ν_{max} (CH_2Cl_2) 3410, 1781, 1734cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.81 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 6.9Hz), 1.18 (1H, m) 1.20 (3H, s) 1.50 (3H, s), 1.44-1.82 (8H, m), 2.11-2.35 (5H, m), 3.37 (1H, dd, *J* 10.6, 6.7Hz), 5.23 (1H, d, *J* 17.4Hz), 5.36 (1H, d, *J* 11.1Hz), 5.82 (1H, d, *J* 8.4Hz), 6.52 (1H, dd, *J* 17.3, 11.0Hz), 7.44 (1H, dd, *J* 7.8, 4.9Hz), 8.12 (2H, br), 8.80 (1H, d, *J* 3.4Hz), 8.99 (1H, d, *J* 1.7Hz); MS (EI) *m/z* 469 (MH^+), Found: 469.2704, $C_{27}H_{37}N_2O_5$ (MH^+) requires 469.2702.

Example 49. Mutilin 14-[*N*-2-furoylcarbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-2-furoylcarbamate]

A mixture of silver cyanate (690 mg, 4.6 mmol), 2-furoyl chloride (0.4 ml, 3.0 mmol), *tetrakis* tripheylphosphine palladium (0) (17 mg, 0.015 mmol)and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) in 1,2-dichloroethane (10 ml) was protected from light and stirred at room temperature under argon for 41 hour. The reaction mixture was filtered through Kieselguhr and concentrated, to afforded a crude product, which was purified by silica gel chromatography to give the title compound (468 mg, 99%); ν_{max} (CH_2Cl_2) 3415, 1777, 1714, 1699cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.42 (4H, m), 1.20 (3H, s), 1.33 (3H, s), 1.53 (2H, m), 1.71 (1H, d, *J* 15.3Hz), 1.75 (1H, d, *J* 11.3Hz), 2.02 (2H, m), 2.20 (1H, m), 2.53 (1H,

dd, *J* 15.4, 10.1Hz), 2.90 (1H, q, *J* 6.4Hz), 3.23 (3H, s), 3.47 (1H, ddd, *J* 11.2, 8.3, 5.3Hz), 5.01 (1H, d, *J* 17.4Hz), 5.30 (1H, d, *J* 10.7Hz), 5.84 (1H, d, *J* 9.9Hz), 6.59 (1H, dd, *J* 3.5, 1.7Hz), 6.73 (1H, dd, *J* 17.4, 10.6Hz), 7.34 (1H, d, *J* 3.3Hz), 7.54 (1H, s), 8.20 (1H, s); MS (CI) *m/z* 471 (M^+).

Step 2. Mutilin 14-[*N*-2-furoylcarbamate]

The product of Step 2 (200 mg, 0.42 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (129 mg, 67%); ν_{max} (CH_2Cl_2) 3412, 1777, 1733, 1716cm^{-1}; ^1H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 7.0Hz), 1.18 (1H, m) 1.19 (3H, s) 1.54 (3H, s), 1.37-1.82 (8H, m), 2.10-2.38 (5H, m), 3.37 (1H, dd, *J* 11.0, 6.6Hz), 5.23 (1H, dd, *J* 17.3, 1.5Hz), 5.38 (1H, dd, *J* 11.0, 1.5Hz), 5.83 (1H, d, *J* 8.5Hz), 6.56 (1H, dd, *J* 17.3, 11.0Hz), 6.57 (1H, dd, *J* 3.5, 1.8Hz), 7.32 (1H, d, *J* 3.3Hz), 7.52 (1H, d, *J* 2.1Hz), 8.15 (1H, s); MS (CI) *m/z* 475 (MNH_4^+).

Example 50. Mutilin 14-[*N*-acetylcarbamate]

Step 1. Acetyl isocyanate

Silver cyanate (690 mg, 4.6 mmol) and acetyl chloride (0.28 ml, 3.94 mmol) in dry dichloromethane (5 ml) were reacted according to the method described in Example 31, Step 1 for 1.75 hours. The solution containing the title compound was immediately used in the next reaction; ν_{max} (CH_2Cl_2) 2257 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-acetylcarbamate]

The solution from step 1 was treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 10 minutes. The title compound was isolated by the same procedure as described in Example 31, Step 2 (420 mg, 100%); ν_{max} (CH_2Cl_2) 3388, 1753, 1713cm^{-1}; ^1H NMR ($CDCl_3$) 0.83 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.54 (6H, m), 1.21 (6H, s), 1.62 (1H, d, *J* 15.7Hz), 1.73 (1H, d, *J* 11.3Hz), 1.99 (2H, m), 2.20 (1H, m), 2.48 (3H, s), 2.49 (1H, dd, *J* 15.4, 10.0Hz), 2.88 (1H, q, *J* 6.4Hz), 3.22 (3H, s), 3.45 (1H, ddd, *J* 11.2, 8.1, 5.3Hz), 5.03 (1H, d, *J* 17.5Hz), 5.33 (1H, d, *J* 10.7Hz), 5.72 (1H, d, *J* 10.0Hz), 6.63 (1H, dd, *J* 17.5, 10.7Hz), 7.45 (1H, s); MS (EI) *m/z* 419 (M^+), Found: 419.2674, $C_{24}H_{37}NO_5$ requires 419.2672.

Step 3. Mutilin 14-[*N*-acetylcarbamate]

The product of Step 2 (284 mg, 0.68 mmol) in dioxane (3 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (190 mg, 69%); ν_{max} (CH_2Cl_2) 3392, 1755, 1734, 1714cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.74 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 7.0Hz), 1.16 (1H, m) 1.19 (3H, s) 1.43 (3H, s), 1.37-1.55 (5H, m),1.59-1.85 (3H, m), 2.05-2.38 (5H, m), 2.42 (3H, s), 3.37 (1H, dd, *J* 10.6, 6.6Hz), 5.23 (1H, dd, *J* 17.4, 1.3Hz), 5.37 (1H, dd, *J* 11.0, 1.3Hz), 5.72 (1H, d, *J* 8.4Hz), 6.49 (1H, dd, *J* 17.4, 11.0Hz), 7.51 (1H, s); MS (CI) *m/z* 423 (MNH_4^+).

Example 51. Mutilin 14-[*N*-(4-chlorobenzenesulphonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (500 mg) in dry dichloromethane (7 ml) was treated with 4-chlorobenzenesulphonamide (265 mg), di*iso*propylethylamine (0.5 ml), and 4-dimethylaminopyridine (10 mg), and the solution was stirred for 30 minutes at room temperature. The solution was diluted with ethyl acetate (50 ml) and washed with dilute HCl (30 ml), water (30 ml), and saturated brine (30 ml). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to yield a white foam (780 mg).

The foam was dissolved in 1,4-dioxane (8 ml) and treated with a saturated solution of zinc chloride in conc. HCl (2.5 ml). The solution was stirred for 2.5 hours at room temperature, and was then diluted with ethyl acetate (50 ml) and washed three times with water. The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to yield a pink foam. Crystallisation from dichloromethane - hexane gave the title compound as colourless crystals (555 mg), m.p. 216 - 218°C; λ_{max} (EtOH) 230 nm (ε 12,100);ν_{max} ($CHCl_3$) 3380, 1735, and 1210 cm^{-1}; δ_H ($CDCl_3$) 7.94 (2H, d, *J* 5 Hz), 7.52 (2H, d, *J* 5 Hz), 6.27 (1H, dd, *J* 17.4 and 11 Hz), 5.61 (1H, d, *J* 8.4 Hz), 5.24 (1H, dd, *J* 11 and 1.2 Hz), 5.10 (1H, dd, *J* 17.4 and 1.2 Hz), 3.30 (1H, dd, *J* 10.1 and 6.7), 2.20 (3H, m), 1.95 (2H, m), 1.8 - 1.0 (overlapping multiplets), 1.34 (3H, s), 1.09 (3H, s), 0.83 (3H, d, *J* 7 Hz), and 0.52 (3H, d, *J* 6.8 Hz); MS (CI) *m/z* 555 ($M.NH_4^+$).

Example 52. Mutilin 14-[*N*-(4-fluorobenzenesulphonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-fluorobenzenesulphonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (200 mg) in dry dichloromethane (3 ml) was treated with 4-fluorobenzenesulphonamide (180 mg), di*iso*propylethylamine (0.2 ml), and 4-dimethylaminopyridine (2 mg), and the solution was stirred for 30 minutes at room temperature. The solution was diluted with ethyl acetate (50 ml) and washed with dilute HCl (20 ml), water (20 ml), and saturated brine (20 ml). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to yield a colourless gum. Chromatography on silica gel using ethyl acetate - hexane gave the title compound as a colourless gum (240 mg); ν_{max} ($CHCl_3$) 3379, 1737, 1697, and 1594 cm^{-1}; MS (EI) *m/z* 535 (M^+) (Found: M^+, 535.2408. $C_{28}H_{38}NO_6FS$ requires *M*, 535.2404).

Step 2. Mutilin 14-[*N*-(4-fluorobenzenesulphonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-fluorobenzenesulphonyl)]-carbamate (200 mg) in 1,4-dioxane (4 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.5 ml) and the solution was kept at room temperature for 1.5 hours. The solution was diluted with ethyl acetate (50 ml) and was washed three times with water (20 ml portions). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to give a colourless gum. Chromatography on silica gel using ethyl acetate - hexane gave the title compound as colourless crystals (140 mg). Recrystallisation from dichloromethane - hexane gave colourless needles, m.p. 228-229°C; λ_{max} (EtOH) 217 nm (ε 11,660); δ_H ($CDCl_3$) 8.01 (2H, dd, *J* 9 and 5 Hz), 7.20 (2H, t, *J* 9 Hz), 6.27 (1H, dd, *J* 17.5 and 11 Hz), 5.58 (1H, d, *J* 8.3 Hz), 5.20 (1H, dd, *J* 11 and 1.2 Hz), 5.06 (1H, dd, *J* 17.5 and 1.2 Hz), 3.20 (1H, d, *J* 6.2 Hz), 2.22 (2H, m), 1.97 (2H, m), 1,8 - 1.0 (overlapping multiplets), 1.35 (3H, s), 1.09 (3H, s), 0.85 (3H, d, *J* 7 Hz), 0.51 (3H, d, *J* 6.7 Hz); MS (CI) *m/z* 539 ($M.NH_4^+$).

Example 53. Mutilin 14-[*N*-(4-*n*-propylbenzenesulphonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-*n*-propylbenzenesulphonyl)]-carbamate

Using the process described in Example 52, Step 1, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (200 mg) and 4-*n*-propylbenzenesulphonamide (150 mg) were converted into the title compound, which was obtained as a colourless gum (220 mg); MS (CI) *m/z* 577 ($M.NH_4^+$).

Step 2. Mutilin 14-[*N*-(4-*n*-propylbenzenesulphonyl)]-carbamate

Using the process described in Example 52, Step 2, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-*n*-propylbenzenesulphonyl)]-carbamate (190 mg) was converted into the title compound, which was obtained as a colourless gum (150 mg); ν_{max} ($CHCl_3$) 3565, 3384, 1735, 1598, and 1421 cm^{-1}; δ_H ($CDCl_3$) 7.85 (2H, d, *J* 8.5 Hz), 7.32 (2H, d, *J* 8.5 Hz), 6.28 (1H, dd, *J* 17.3 and 11 Hz), 5.61 (1H, d, *J* 8.3 Hz), 5.23 (1H, dd, *J* 11 and 1.3 Hz), 5.08 (1H, dd, *J* 17 and 1.3 Hz), 3.29 (1H, dd, *J* 10.2 and 6.6 Hz), 2,67 (2H, t, *J* 7.3 Hz), 2.20 (2H, m), 1.95 (2H, m), 1.8 - 0.8 (overlapping multiplets), 0.49 (3H, d, *J* 6.7 Hz); MS (CI) *m/z* 563 ($M.NH_4^+$).

Example 54. Mutilin 14-[*N*-(4-hydroxybenzenesulphonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (300 mg) in dry dichloromethane (5 ml) was treated with 4-hydroxybenzenesulphonamide (170 mg), di*iso*propylethylamine (0.35 ml), and 4-dimethylaminopyridine (8 mg), and the solution was stirred for 30 minutes at room temperature. The solution was diluted with ethyl acetate (50 ml) and washed with dilute HCl (20 ml), water (20 ml), and saturated brine (20 ml). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to yield a colourless gum. Chromatography on silica gel using ethyl acetate - hexane gave the product as a white foam (410 mg).

The above product was dissolved in 1,4-dioxane (8 ml) and the solution was treated with a saturated solution of zinc chloride in conc. HCl (3 ml); the solution was kept at room temperature for 3.5 hours. The solution was diluted with ethyl acetate (50 ml) and was washed three times with water (20 ml portions). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to give a pale yellow gum. Chromatography on silica gel

using ethyl acetate - hexane gave the product as a white foam (180 mg). The NMR spectrum of this product showed that it contained two different mutilin moieties, and suggested that it had been derived by simultaneous reaction of 4-*epi*-mutilin chloroformate molecules with both the hydroxyl and the sulphonamido groups of 4-hydroxybenzenesulphonamide:

[mutilin]—$O_2CO.C_6H_4.SO_2NHCO_2$—[mutilin]

The above product was dissolved in methanol (8ml) and the solution was treated with 1*M* NaOH (1ml) and kept at room temperature for 6 hours. The solution was diluted with ethyl acetate (50 ml) and was washed with dilute HCl (20 ml) and saturated brine (20 ml). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to give a yellow gum. Chromatography on silica gel using ethyl acetate - hexane gave the title compound as a white solid (107 mg); λ_{max} (EtOH) 239 nm (ε 12,340); ν_{max} ($CHCl_3$) 3690, 3583, 3382, 1734, 1602, 1418, and 1157 cm^{-1}; δ_H ($CDCl_3$ - d_4-MeOH) 7.77 (2H, d, *J* 7 Hz), 6.84 (2H, d, *J* 7 Hz), 6.28 (1H, dd, *J* 17.3 and 11 Hz), 5.56 (1H, d, *J* 8.3 Hz), 5.21 (1H, d, *J* 11 Hz), 5.07 (1H, d, *J* 17.3 Hz), 3.26 (1H, d, *J* 6.4 Hz), 2.5 - 1.0 (overlapping multiplets), 0.82 (3H, d, *J* 7 Hz), 0.51 (3H, d, *J* 6.5 Hz); MS (CI) *m/z* 537 ($M.NH_4^+$), 519 . (M^+).

Example 55. Mutilin 14-[*N*-(3,4-dimethoxybenzoyl)carbamate]

Step 1. 3,4-Dimethoxybenzoylisocyanate

Silver cyanate (690 mg, 4.6 mmol) and 3,4-dimethoxybenzoylchloride (800mg, 4.0 mmol) in dry dichloromethane (5 ml) were reacted according to the method described in Example 31, Step 1. The solution containing the title compound was immediately used in the next reaction; ν_{max} (CH_2Cl_2) 2238 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3,4-dimethoxybenzoyl)carbamate]

The solution from step 1 was treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 40 minutes. The title compound was isolated by the same procedure as described in Example 31, Step 2 (392 mg, 72%); ν_{max} (CH_2Cl_2) 3430, 1774, 1698cm^{-1}; ^1H NMR ($CDCl_3$) 0.91 (3H, d, *J* 6.8Hz), 1.00 (3H, d, *J* 6.4Hz), 1.05-1.57 (6H, m), 1.21 (3H, s), 1.34 (3H, s), 1.73 (1H, d, *J* 15.3Hz), 1.75 (1H, d, *J* 10.5Hz), 2.02 (2H,

m), 2.20 (1H, m), 2.54 (1H, dd, *J* 15.2, 10.1Hz), 2.91 (1H, q, *J* 6.2Hz), 3.23 (3H, s), 3.47 (1H, m), 3.95 (6H, s), 5.02 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 9.9Hz), 6.79 (1H, dd, *J* 17.5, 10.7Hz), 6.90 (1H, d, *J* 8.4Hz), 7.34 (1H, dd, *J* 8.4, 2.0Hz), 7.46 (1H, d, *J* 2.0Hz), 7.94 (1H, s); MS (CI) *m/z* 542 (MH^+).

Step 3. Mutilin 14-[*N*-(3,4-dimethoxybenzoyl)carbamate]

The product of Step 2 (275 mg, 0.51 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (75 mg, 28%); ν_{max} (KBr disc) 3305, 1768, 1730, 1687cm^{-1}; ^1H NMR ($CDCl_3$) 0.82 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 6.9Hz), 1.20 (1H, m), 1.23 (3H, s), 1.54 (3H, s), 1.44-1.82 (8H, m), 2.12-2.38 (5H, m), 3.38 (1H, dd, *J* 10.7, 6.6Hz), 3.94 (6H, s), 5.24 (1H, dd, *J* 17.4, 1.4Hz), 5.38 (1H, dd, *J* 10.9, 1.4Hz), 5.84 (1H, d, *J* 8.5Hz), 6.58 (1H, dd, *J* 17.3, 11.0Hz), 6.88 (1H, d, *J* 8.4Hz), 7.30 (1H, dd, *J* 8.4, 2.0Hz), 7.43 (1H, d, *J* 2.1Hz), 7.86 (1H, s); MS (EI) *m/z* 527 (M^+), Found: 527.2884, $C_{30}H_{41}NO_7$ requires 527.2883.

Example 56. Mutilin 14-[*N*-(3,4-methylenedioxybenzoyl)carbamate]

Step 1. 3,4-Methylenedioxybenzoylisocyanate

Silver cyanate (690 mg, 4.6 mmol) and piperonyloyl chloride (738mg, 4.0 mmol) in dry dichloromethane (5 ml) were reacted according to the method described in Example 31, Step 1. The solution containing the title compound was immediately used in the next reaction; ν_{max} (CH_2Cl_2) 2238 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3,4-methylenedioxybenzoyl)carbamate]

The solution from step 1 was treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1.0 mmol) and the reaction stirred for 40 minutes. The title compound was isolated by the same procedure as described in Example 31, Step 2 (283 mg, 54%); ν_{max} (CH_2Cl_2) 3428, 1775, 1698cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.56 (6H, m), 1.20 (3H, s), 1.31 (3H, s), 1.71 (1H, d, *J* 15.3Hz), 1.75 (1H, d, *J* 11.2Hz), 1.99 (2H, m), 2.20 (1H, m), 2.52 (1H, dd, *J* 15.2, 10.1Hz), 2.90 (1H, q, *J* 6.5Hz), 3.23 (3H, s), 3.46 (1H, ddd, *J* 11.2, 8.2, 5.3Hz), 5.01 (1H, d, *J* 17.4Hz), 5.29 (1H, d, *J* 10.7Hz), 5.84 (1H, d, *J* 10.0Hz), 6.07 (2H, s), 6.72 (1H, dd, *J* 17.5, 10.7Hz), 6.87

(1H, d, *J* 8.0Hz), 7.32 (1H, d, *J* 1.5Hz), 7.36 (1H, dd, *J* 7.9, 1.8Hz), 7.89 (1H, s); MS (CI) *m/z* 543 (MNH_4^+), 526 (MH^+).

Step 3. Mutilin 14-[*N*-(3,4-methylenedioxybenzoyl)carbamate]

The product of Step 2 (237 mg, 0.45 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound (151 mg, 65%); ν_{max} (CH_2Cl_2) 3432, 1777, 1733, 1712cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.18 (1H, m), 1.19 (3H, s), 1.38-1.83 (8H, m), 1.51 (3H, s), 2.09-2.37 (5H, m), 3.37 (1H, dd, *J* 10.9, 6.6Hz), 5.23 (1H, dd, *J* 17.4, 1.5Hz), 5.38 (1H, dd, *J* 11.0, 1.5Hz), 5.82 (1H, d, *J* 8.5Hz), 6.06 (2H, s), 6.56 (1H, dd, *J* 17.4, 11.0Hz), 6.85 (1H, d, *J* 8.0Hz), 7.29 (1H, d, *J* 1.6Hz), 7.32 (1H, dd, *J* 8.1, 1.8Hz), 7.81 (1H, s); MS (EI) *m/z* 511 (M^+), Found: 511.2566, $C_{29}H_{37}NO_7$ requires 511.2570.

Example 57. Mutilin 14-(*N*-*p*-methoxysulphonylcarbamate)

Step 1. Mutilin 11-dichloroacetate

Mutilin (1.0 g, 3.12 mmol) was disolved in dry THF (10 ml) under argon and treated with pyridine (0.33 ml, 4.06 mmol), dichloroacetic anhydride (820 mg, 3.42 mmol) in THF (2 ml), and *N,N*-4-dimethylaminopyridine (5mg). After 24 hours the reaction was diluted with ethyl acetate, washed with 1M hydrochloric acid, saturated sodium hydrogen carbonate and saturated sodium chloride solutions. The solution was dried over magnesium sulphate and concentrated to afford the crude product (1.5g). Purification by silica gel chromatography (15-25% ethyl acetate / hexane) afforded the *title* compound (925 mg, 69%); ν_{max} (CH_2Cl_2) 3635, 1756, 1735cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.86 (3H, d, *J* 7.1Hz), 0.97 (3H, d, *J* 7.0Hz), 1.06 (3H, s), 1.15 (1H, m), 1.32-1.50 (4H, m), 1.39 (3H, s), 1.63-2.02 (5H, m), 2.10 (1H, s), 2.22 (2H, m), 2.37 (1H, quintet, *J* 7.0Hz), 4.31 (1H, t, *J* 6.4Hz), 4.91 (1H, d, *J* 6.9Hz), 5.32 (1H, dd, *J* 11.2, 0.7Hz), 5.48 (1H, dd, *J* 17.7, 0.8Hz), 6.00 (1H, s), 6.12 (1H, dd, *J* 18.0, 11.2Hz); MS (CI) *m/z* 448 / 450 / 452 (MNH_4^+).

Step 2. Mutilin 14-chloroformate-11-dichloroacetate

The product of Step 1 (882 mg, 2.04 mmol) was disolved in dry THF (15 ml) under argon, cooled in an ice-bath, and treated with trichloromethyl chloroformate (0.25 ml, 2.07 mmol) and pyridine (0.21 ml, 2.6 mmol). The resultant heterogeneous mixture was rapidly stirred for 1 hour, diluted with ethyl acetate and washed with saturated sodium chloride solution. The solution was

dried over magnesium sulphate and concentrated to afford the *title* compound which was used without purification (982 mg, 97%); ν_{max} (CH_2Cl_2) 1760, 1737cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.83 (3H, d, *J* 7.1Hz), 0.88 (3H, d, *J* 7.1Hz), 1.13 (3H, s), 1.16 (1H, m), 1.37-1.54 (3H, m), 1.48 (3H, s), 1.61-1.92 (4H, m), 2.13-2.37 (4H, m), 2.46 (1H, quintet, *J* 7.0Hz), 4.93 (1H, t, *J* 6.8Hz), 5.31 (1H, d, *J* 17.2Hz), 5.37 (1H, d, *J* 10.7Hz), 5.61 (1H, d, *J* 8.4Hz), 5.99 (1H, s), 6.25 (1H, dd, *J* 17.5, 11.2Hz); MS (EI) *m/z* 498-492 (M^+).

Step 3. Mutilin 11-dichloroacetate-14-(*N*-*p*-methoxysulphonylcarbamate)

The product of Step 2 (250 mg, 0.51 mmol) was disolved in dichloromethane (5 ml) under argon and treated with *p*-methoxysulphonamide (187 mg, 1.0 mmol) in DMF (0.5 ml), *N,N*- di*iso*propylethylamine (0.2 ml, 1.15 mmol) and N,N-4-dimethylaminopyridine (5mg). After stirring at room temperature for 3 hours the solution was diluted with dichloromethane and washed with 1M hydrochloric acid. The solution was dried over magnesium sulphate and concentrated to afford the crude product (746 mg). Purification by silica gel chromatography (50% ethyl acetate / hexane) afforded the *title* compound (294 mg, 90%); ν_{max} (CH_2Cl_2) 3368, 1736cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.53 (3H, d, *J* 6.7Hz), 0.83 (3H, d, *J* 7.0Hz), 0.99 (3H, s), 1.06-1.89 (8H, m), 1.35 (3H, s), 1.94-2.29 (4H, m), 2.45 (1H, m), 3.88 (3H, s), 4.86 (1H, d, *J* 6.8Hz), 5.09 (1H, d, *J* 17.6Hz), 5.19 (1H, d, *J* 11.2Hz), 5.52 (1H, d, *J* 8.0Hz), 5.96 (1H, s), 6.16 (1H, dd, *J* 17.6, 11.2Hz), 6.99 (2H, d, *J* 8.9Hz), 7.94 (2H, d, *J* 8.9Hz); MS (CI) *m/z* 665 / 663 / 661(MNH_4^+).

Step 4. Mutilin 14-(*N*-*p*-methoxysulphonylcarbamate)

The product of Step 3 (262 mg, 0.41 mmol) was disolved in THF (3 ml) and methanol (1 ml) and treated with 1M sodium hydroxide (1 ml, 1.0 mmol). After 1 hour the solution was diluted with ethyl acetate and washed with 1M hydrochloric acid and water. The solution was dried over magnesium sulphate and concentrated to afford the crude product (260 mg). Purification by silica gel chromatography (50% ethyl acetate / hexane) afforded the title compound (206 mg, 95%); ν_{max} (CH_2Cl_2) 3367, 1736cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.53 (3H, d, *J* 6.7Hz), 0.83 (3H, d, *J* 7.0Hz), 1.08 (1H, m), 1.10 (3H, s), 1.25-1.75 (8H, m), 1.35 (3H, s), 1.97 (2H, m), 2.20 (3H, m), 3.29 (1H, dd, *J* 10.2, 6.6Hz), 3.88 (3H, s), 5.09 (1H, dd, *J* 17.4, 1.3Hz), 5.24 (1H, d, *J* 11.0, 1.2Hz), 5.61 (1H, d, *J* 8.4Hz), 6.28 (1H, dd, *J* 17.4, 11.0Hz), 6.98 (2H, d, *J* 9.0Hz), 7.43 (1H, s), 7.93 (2H, d, *J* 9.0Hz); MS (CI) *m/z* 551(MNH_4^+); (Found: C, 63.13; H, 7.54; N, 2.61. $C_{28}H_{39}NO_7S$ requires C, 63.02; H, 7.37; N, 2.62).

Example 58. Mutilin 14-[*N*-(4-hydroxybenzoyl)carbamate]

Step 1. 11-*O*-Dichloroacetylmutilin

Mutilin (4.0 g, 12.5 mmol) was dissolved in dry tetrahydrofuran (20 ml) and treated with pyridine (1.31 ml, 16.2 mmol), dichloroacetic anhydride (3.29 g, 13.7 mmol), and *N,N*-dimethylaminopyridine (20 mg). The reaction was stirred under argon for 2h at room temperature. Reaction mixture partitioned between ethyl acetate and water. The organic phase was washed with 1.0M HCl, water and saturated sodium chloride solution before drying ($MgSO_4$). Purification was accomplished by chromatography on silica gel. The product was isolated as a crystalline solid (3.57g, 66%); ν_{max} (CH_2Cl_2) 3635, 2936, 1756, 1735 and 1463; ^1H NMR ($CDCl_3$) 0.86 (3H, d, *J* 7.1Hz), 0.97 (3H, d, *J* 7.0Hz), 1.06 (3H, s), 1.15 (1H, m) 1.39 (3H, s), 1.32-1.50 (4H, m), 1.63-2.02 (5H, m), 2.10(1H, s), 2.22 (2H, m), 2.37 (1H, quint., *J* 6.5Hz), 4.31 (1H, t, *J* 6.4Hz), 4.91 (1H, d, *J* 6.9Hz), 5.32 (1H, dd, *J* 11.2, 0.7Hz), 5.48 (1H, dd, *J* 17.7, 0.7Hz), 6.00 (1H, s), 6.12 (1H, dd, *J* 18.0, 11.2Hz); MS (NH3DCI) *m/z* 448,450,452 (MNH_4^+).

Step 2. 11-*O*-Dichloroacetylmutilin-14-[*N*-(4-acetoxybenzoyl)carbamate]

A solution of 4-acetoxybenzoylisocyanate (6 mmol) in dichloroethane (20 ml) (prepared as described in Example 33, Step 1) was treated with 11-*O*-dichloroacetylmutilin (650 mg, 1.5 mmol) and the title compound isolated as described in Example 31, Step 2 (716 mg, 72%): ν_{max} (CH_2Cl_2) 3420, 2943, 1779, 1734, 1604 and 1479; ^1H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.5Hz), 0.87 (3H, d, *J* 7.0Hz), 1.11-1.23 (4H, m), 1.38-1.93 (11H, m), 2.14-2.32 (5H, m), 2.56-2.62 (1H, m), 4.96 (1H, d, *J* 6.7Hz),, 5.33 (1H, d, *J* 17.6Hz), 5.36 (1H, dd, *J* 11.1Hz), 5.75 (1H, d, *J* 8.1Hz), 5.99 (1H, s), 6.44 (1H, dd, *J* 17.3, 11.3Hz), 7.22 (2H, d, *J* 8.7Hz),), 7.84 (2H, d, *J* 8.7Hz), 7.89 (1H, bs): MS (ESI, +ve ion) *m/z* 653 (MNH_4^+); (Found: C, 60.34; H, 6.42; N, 2.13. $C_{32}H_{39}Cl_2NO_8$ requires C, 60.38; H, 6.18; N, 2.20)

Step 3. Mutilin 14-[*N*-(4-hydroxybenzoyl)carbamate]

11-*O*-Dichloroacetylmutilin-14-[*N*-(4-acetoxybenzoyl)carbamate] (671 mg, 1.05 mmol) was dissolved in tetrahydrofuran (5 ml) and methanol (1.0 ml) before treating with 1.0M sodium hydroxide (3.2 ml, 3.2 mmol). The reaction was stirred at room temperature for 1h. The reaction was partitioned between ethyl acetate and 1.0M HCl and the organic phase washed with water, sodium hydrogen carbonate solution, and finally brine. After drying ($MgSO_4$) the crude product was purified by chromatography on silica gel, loading and eluting with 50% ethyl

acetate in hexane followed by ethyl acetate. The title compound was isolated as a solid (409 mg, 80%).

Example 59. Mutilin 14-[N-(4-hydroxymethylbenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxymethylbenzoyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-formylbenzoyl)carbamate] (250 mg, 0.49 mmol) (prepared as described in Example 42, Step 1) was dissolved in dry tetrahydrofuran (2.5 ml) and treated with di*iso*butyl aluminium hydride (0.54 ml of 1.0M solution in toluene, 0,8 mmol). After stirring at room temperature for 15 minutes the reaction was partitioned between ethyl acetate and water. After washing the organic phase with water, saturated sodium hydrogen carbonate solution and brine the solution was dried ($MgSO_4$). Purifcation was accomplished by chromatography on silica gel eluting with mixtures of ethyl acetate in hexane. The title compound was isolated as a foam (184 mg, 73%); ν_{max} (CH_2Cl_2) 3605, 3426, 2930, 1776, 1731, 1698, 1613, and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.00 (3H, d, *J* 6.4Hz), 1.31 (3H, d, *J* 6.8Hz), 1.07-1.60 (12H, m), 1.69-1.73 (2H, m), 1.91-2.04 (2H, m), 2.15-2.24 (1H, m), 2.53 (1H, dd, *J* 15.2, 10.1Hz), 2.90 (1H, q, *J* 6.3Hz), 3.22 (3H, s), 3.42-3.50 (1H, m), 4,79 and 4.81 (2H, s+s), 5.00 (1H, d, *J* 17.4Hz), 5.30 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 9.9Hz), 6.72 (1H, dd, *J* 17.4, 10.7Hz), 7.49 (2H, d, *J* 8.2Hz), 7.82 (1H, d, *J* 8.3Hz), 8.00 (1H, bs); MS (NH_3DCI) *m/z* 512 (MH^+), *m/z* 529 (MNH_4^+)

Step 2. Mutilin 14-[*N*-(4-hydroxymethylbenzoyl)carbamate]

The product of Step 1 (164 mg, 0.32 mmol) in dioxane (2.0 ml) was treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml), as for Example 1 Step 2, to afford the title compound (52 mg, 33%); ν_{max} (CH_2Cl_2) 3604, 3431, 1778, 1733, 1714, and 1613cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.81 (3H, d, *J* 6.6Hz), 0.88 (3H, d, *J* 7.0Hz), 1.19-1.81 (16H, m), 1.86 (1H, bs), 2.10-2.37 (4H, m), 3.37 (1H, dd, *J* 10.5, 6.5Hz), 4.79 (2H, bs), 5.23 (1H, dd, *J* 17.4, 1.4Hz), 5.38 (1H, dd, *J* 11.0, 1.4Hz), 5.83 (1H, d, *J* 8.5Hz), 6.55 (1H, dd, *J* 17.3, 11.0Hz), 7.50 (1H, d, *J* 8.2Hz), 7.80 (1H, d, *J* 8.3Hz), 7.96 (1H, bs); MS (NH_3DCI) *m/z* 498 (MH^+), *m/z* 515 (MNH_4^+).

Example 60. Mutilin 14-[N-(4-methanesulfonamidobenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-aminobenzoyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-nitrobenzoyl)carbamate] (460 mg, 0.87 mmol) was converted to the title compound by the method described in Example 34 (268 mg, 64%): ν_{max} (CH_2Cl_2) 3405, 2930, 1771, 1698, 1623, and 1477cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.07-1.61 (12H, m), 1.69-1.76 (2H, m), 1.94-2.04 (2H, m), 2.15-2.24 (1H, m), 2.52 (1H, dd, *J* 15.2, 10.1Hz), 2.91 (1H, q, *J* 6.4Hz), 3.22 (3H, s), 3.42-3.50 (1H, m), 4.15 (2H, bs), 5.00 (1H, d, *J* 17.5Hz), 5.29 (1H, d, *J* 10.7Hz), 5.83 (1H, d, *J* 9.9Hz), 6.64-6.80 (3H, m), 7.66 (2H, d, *J* 8.6Hz), 7.86 (1H, bs); MS (NH_3DCI) *m/z* 497 (MH^+).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-methanesulfonamidobenzoyl)carbamate]

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-aminobenzoyl)carbamate] (248 mg, 0.50 mmol) was dissolved in dry dichloromethane (5 ml) whilst under argon at room temperature. The reaction was treated with pyridine (0.132 ml, 1.65 mmol) and methanesulfonyl chloride (0.126 ml, 1.65 mmol) which were added in three separate portions over a period of 3h. The reaction was diluted with dichloromethane and washed with saturated sodium hydrogen carbonate, 1.0M HCl, water, and saturated sodium chloride solution before drying ($MgSO_4$). The crude material was triturated with hexane to give the title compound as a solid (236 mg, 82%); ν_{max} (KBr disc) 1762, 1695, 1603cm^{-1}; ^{1}H NMR (d_6-acetone) 0.94 (3H, d, *J* 6.9Hz), 1.01 (3H, d, *J* 6.4Hz), 1.0-1.97 (12H, m), 2.04-2.10 (m, obscured by solvent), 2.53 (1H, dd, *J* 15.6, 10.5Hz), 2.80-3.00 (m, obscured by solvent), 3.11 (3H, s), 3.21 (3H, s), 3.46-3.52 (1H, m), 4.99 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.7Hz), 5.80 (1H, d, *J* 9.9Hz), 6.82 (1H, dd, *J* 17.5, 10.7Hz), 7.43 (2H, d, *J* 8.8Hz), 7.94 (2H, d, *J* 8.7Hz), 9.11 (1H, bs), 9.91 (1H, s).

Step 3: Mutilin 14-[N-(4-methanesulfonamidobenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-methanesulfonamidobenzoyl)carbamate] (208 mg, 0.36 mmol) was dissolved in dioxan (2.0 ml) and treated with a saturated solution of zinc chloride in conc. HCl (0.5 ml), as for Example 1 Step 2, to afford the title compound (72 mg, 36%);

ν_{max} (KBr disc) 1733 and 1608cm^{-1}; ^{1}H NMR (d_6-acetone) 0.67 (3H, d, *J* 6.3Hz), 0.82 (3H, d, *J* 7.1Hz), 0.91-1.71 (15H, m), 1.96-2.05(1H, m), 2.19 (1H, quint., *J* 6.8Hz), 2.26 (1H, bs), 2.96 (3H, s), 3.30 (1H, d, *J* 7.3Hz, ex. in D_2O), 3.50 (1H, m, collapse to d in D_2O, *J* 5.9Hz), 5.05 (1H, dd, *J* 11.0, 1.7Hz), 5.11 (1H, dd, *J* 17.7, 1.7Hz), 5.64 (1H, d, *J* 8.3Hz), 6.32 (1H, dd, *J* 17.7, 11.1Hz), 7.26 (1H, d, *J* 8.8Hz), 7.80 (1H, d, *J* 8.7Hz), 9.72 (1H, bs, ex in D_2O); MS (NH_3DCI) *m/z* 561 (MH^+), *m/z* 578 (MNH_4^+).

Example 61. Mutilin 14-[*N*-(4-Aminosulphonylphenyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-aminosulphonylphenyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (336 mg, 1 mmol) in dry CH_2Cl_2 (7.5 ml) was treated with 4-chlorosulphonylphenyl isocyanate (283 mg, 1.3 mmol) and *N,N*-di-iso-propylethylamine (1 drop) and the solution was kept at room temperature, with exclusion of moisture, for 2 days, and then in a refrigerator for 70 h. The solvent was then removed using a rotary eveporator and replaced by tetrahydrofuran (7.5 ml). 0.880 S.G. Aqueous ammonia (0.5 ml) was then added and the mixture was stirred for 1.5 h. The solution was diluted with ethyl acetate (50 ml) and was washed with brine. The aqueous layer was re-extracted with ethyl acetate (50 ml) and the combined ethyl acetate solutions were washed with 1M HCl (5ml) / brine (15 ml). The solution was dried ($MgSO_4$) and the solvent was removed by evaporation under reduced pressure to yield a colourless foam. The foam was chromatographed on silica gel, using 4:6, followed by 1:1, followed by 7:3 ethyl acetate - hexane, to give (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-aminosulphonylphenyl)]-carbamate as a colourless solid foam (460 mg, 86%); ν_{max} (CH_2Cl_2) 3420, 3335, 2980, 2930, 1731, 1698, 1592, 1218, and 1163 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.87 (3H, d, *J* 6.9 Hz), 1.00 (3H, d, *J* 6.37 Hz), 1.01-1.8 (*ca* 14 H, m), 1.9 - 21. (2H, m), 2.1 - 2.3 (1H, m), 2.50 (1H, dd, *J* 10.0, 15.2 Hz), 2.94 (1H,q, *J* 6.4 Hz), 3.23 (3H, s), 3.4 - 3.6 (1H, m), 4.84 (2H, s), 5.03 (1H, d, *J* 17.5 Hz), 5.34 (1H, d, *J* 10.7 Hz), 5.81 (1H, d, *J* 9.8 Hz), 6.70 (1H, dd, *J* 10.6, 17.5 Hz), 6.88 (1H, s), 7.59 (2H, d, *J* 8.7 Hz), 7.88 (2H, d, *J* 8.8 Hz); MS (CI) *m/z* 550 $(MNH_4)^+$.

Step 2. Mutilin 14-[*N*-(4-Aminosulphonylphenyl)]-carbamate

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin [*N*-(4-aminosulphonylphenyl)]-carbamate (410 mg, 0.77 mmol) in dioxane (7.5 ml) was treated with a

saturated solution of zinc chloride in conc. HCl (1 ml) and the solution was stirred at room temperature for 5 hours. As the reaction had not proceded to completion more of a saturated solution of zinc chloride in conc. HCl (2 ml) was added and stirring was continued for 2 h. The mixture was diluted with ethyl acetate (50 ml) and the solution was washed with saturated NaCl solution (20 ml) and saturated $NaHCO_3$ solution (20 ml). The solution was dried ($MgSO_4$) and the solvent was removed by evaporation under reduced pressure to yield a colourless solid. The solid was chromatographed on silica gel, loading in CH_2Cl_2 / toluene containing a trace of ethyl acetate and using 1:1 ethyl acetate - hexane, followed by ethyl acetate - toluene mixtures; 3:7; followed by 6:4; followed by 1:1; to give mutilin [*N*-(4-aminosulphonylphenyl)]-carbamate as a colourless solid (281 mg, 70%); ν_{max} (KBr) 1725, 1595, 1530, 1337, 1317, 1228 and 1160 cm^{-1}; ^1H NMR [$(CD_3)_2SO$] 0.90 (3H, d, *J* 6.8 Hz), 1.00 (3H, d, *J* 6.3 Hz), 1.0 - 1.8 (14 H, m, including singlets at 1.08 and 1.43), 2.04 - 2.27 (4H, m), 2.42 (1h, br s), 3.45 (1H, br t, *J ca.* 5.8 Hz; d, *J* 5.5 Hz after D_2O exch.), 4.52 (1H, d, *J* 6.1 Hz, exch D_2O), 5.05 - 5.15 (2H, m), 5.38 (1H, br d, *J* 7.8 Hz), 6.27 (1H, dd, *J* 11.1, 17.7 Hz), 7.21 (2H, s, exch D_2O), 7.59 (2H, d, *J* 8.8 Hz), 7.71 (2H, d, *J* 8.8 Hz), 9.82 (1H, s); MS(CI) *m/z* 536 ($M + NH_4^+$).

Example 62. Mutilin 14-{*N*-[4-([2*R*]-2,3-dihydroxypropyloxy)-benzoyl]}-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxybenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-acetoxybenzoyl)]-carbamate (Example 37, Step 2) (809 mg, 1.5 mmol) in 1,4-dioxan (10 ml) was treated with aqueous 1M NaOH (4.5 ml) and the mixture was stirred for 2.5 h. Ethyl acetate (100ml) and aqueous 1M HCl (10 ml), followed by water (50 ml) were added. After separation of the layers the aqueous layer was washed with ethyl acetate. The combined ethyl acetate layers were dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel, loading with CH_2Cl_2, and eluting with ethyl acetate / hexane mixtures: 1:1, folowed by 6:4, followed by 7:3, followed by 8:2, to give the title compound (677 mg, 90%) as a colourless solid; ν_{max} (CH_2Cl_2) 3565, 3417, 2930, 1774, 1729, 1698, 1608, 1478, 1187, and 1167 cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8 Hz), 1.00 (3H, d, *J* 6.3 Hz), 1.0 - 1.8 (14 H, m, including s at 1.20 and s at 1.31), 1.99 (2H, m), 2.21 (1H, dt, *J* 10.0, 2.7 Hz), 2.52 (1h, dd, *J* 10.1, 15.2 Hz), 2.91 (1H, q, *J* 6.4 Hz), 3.23 (3H, s), 3.46 (1H, m), 5.01 (1H, d, *J* 17.5 Hz), 5.28 (1H, d, *J* 10.8 Hz), 5.84 (1H, d, *J* 9.9 Hz), 6.71 (1H, dd, *J* 10.7, 17.5 Hz), 6.94

(2H, d, *J* 8.7 Hz), 7.75 (2H, d, *J* 8.7 Hz), 7.96 (1H, s); MS(CI) *m/z* 498 (MH^+), 515 (MNH_4^+).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[4-([2*R*]-2,3-dihydroxypropyloxy)-benzoyl]}-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxybenzoyl)]-carbamate (497 mg, 1 mmol) in *tert*-butanol (5 ml) under an atmosphere of argon was warmed to effect dissolution, and then treated with sodium hydride (40 mg of a 60% dispersion in oil, 1 mmol). When effervescence had ceased (*ca.* 30 min) (*R*)-(+)-glycidol (0.06 ml, 74 mg, 1 mmol) in dichloromethane (2.5 ml) was added, followed by titanium(IV) isopropoxide (0.36 ml, 341 mg, 1.2 mmol). The mixture was strirred under an argon atmosphere for 18 h , and then heated under reflux (oil bath 50°) for 6.5 h. Ethyl acetate (50 ml) / 1M HCl (25 ml) were added the layers separated. The aqueous layers was re-extracted with ethyl acetate and combined ethyl acetate layers were washed with brine and dried ($MgSO_4$). After removal of solvent the crude product was chromatographed on silica gel, loading in CH_2Cl_2, and eluting with ethylacetate / hexane mixtures: 1:1, follwed by 6:4, followed by 7:3, followed by 8:4. Fractions containing the product were combined and evaporated to give the title compound as a solid foam (297 mg, 52%); ν_{max} (CH_2Cl_2) 3585, 2931, 1774, 1729, 1698, 1605, 1478, and 1171 cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8 Hz), 1.00 (3H,d, *J* 6.3 Hz), 1.0 -1.6 (12H, m, including s at 1.20 and s at 1.30) 1.70 (1H, d, *J* 9.9 Hz), 1.70 (1H, d, *J* 5.7 Hz), 1.9 - 2.3 (4H, m; 1H exch. D_2O), 2.53 (1H, dd, *J* 10.1, 15.2 Hz), 2.60 (1H, br s, exch. D_2O), 2.90 (1H, q, *J* 6.4 Hz), 3.22 (3H, s), 3.41 - 3.50 (1H, m), 3,7 - 4.0 (2H, m, signal sharpens on D_2O exch.), 4.07 - 4.16 (3H, m), 5.01 (1H, d, *J* 17.4 Hz), 5.29 (1H, d, *J* 17.4 Hz), 5.29 (1H, *J* 10.8 Hz), 5.84 (1H, d *J* 9.9Hz), 6.71 (1H, dd, *J* 10.6, 17.4 Hz), 6.97 (2H, d, *J* 8.8 Hz), 7.79 (2H, d, *J* 8.8 Hz), 8.00 (1H, s); MS (Electrospray) *m/z* 572 (MH^+), 1143 $(2M+H)^+$.

Step3. Mutilin 14-{*N*-[4-([2*R*]-2,3-dihydroxypropyloxy]-benzoyl]}-carbamate

The product of Step 2 (256 mg, 0.45 mmol) in dioxane (3ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.0 ml), as for Example 1 Step 2, to afford the title compound (105 mg, 42%); ν_{max} (KBr) 1761, 1732, 1605, 1497, 1255, 1204, and 1174 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OH) 0.77 (3H, d, *J* 6.4 Hz) 0.85 (3H, d, *J* 6.9 Hz), 1.0 - 2.4 (19 H, m, including s at 1.15 and s at 1.48), 3.33 (1h, d, *J* 6.5 Hz), 3.60 - 3.83 92h, m), 3.9 - 4.2 (3H, m), 5.19 (1H, dd, *J* 1.4, 17.4 Hz), 5.33 (1H, dd, *J* 1.3, 11.0 Hz), 5.78 (1H, d, *J* 8.3 Hz), 6.51 (1h, dd, *J*

11.0, 17.3 Hz), 6.92 (2H, d, *J* 8.8 Hz), 7.74 (2H, d, *J* 8.8 Hz); MS (Electrospray) *m/z* 558 (MH^+), 1115 ($2M+H^+$).

Example 63. Mutilin 14-(*N*-Chloroacetyl)-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-chloracetyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335mg, 1.0mmol) and silver cyanate (225 mg, 1.5 mmol) in dichloromethane (5 ml) under an argon atmosphere in a flask wrapped in aluminium foil was treated with chloroacetyl chloride (0.12 ml, 169 mg, 1.5 mmol), and the mixture was stirred for 1 h. The mixture was filtered through kieselguhr and evaporated. Toluene was then added and removed. The residue was chromatographed on silica gel, loading in dichloromethane and eluting with ethyl acetate / hexane mixtures: 2:8, followed by 3:7 to give the title compound (456 mg, quant.); ν_{max} (CH_2Cl_2) 3381, 2981, 1787, 1754, 1728, 1698, 1489, 1459, and 1198 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83 (3H, d, *J* 6.8 Hz), 1.00 (3H, d, *J* 6.4 Hz), 1.01 - 1.40 (10H, m, including s at 1.20 and s at 1.23), 1.40 - 1.56 (2H, m), 1.62 (1H, d, *J* 15.3 Hz), 1.73 (1H, d, *J* 11.3 Hz), 1.8 - 2.1 (2H, m), 2.20 (1H, dt, *J* 2.8, 12.7 Hz), 2.51 (1H, dd, *J* 10.1, 15.3 Hz), 2.86 (1H, q, *J* 6.3 Hz), 3.22 (3H, s), 3.35 - 3.50 (1H, m), 4.51 (2H, s), 5.03 (1H, d, *J* 17.5 Hz), 5.32 (1H, d, *J* 10.7 Hz), 5.75 (1H, d, *J* 10.0 Hz) 6.60 (1H, dd, *J* 10.7, 17.5 Hz), 7.88 (1H, s, exch D_2O); MS(CI) *m/z* 471 (MNH_4^+).

Step 2. Mutilin 14-(*N*-Chloroacetyl)-carbamate

The product of Step 2 (400 mg, 0.88 mmol) in dioxane (4.5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.5 ml), as for Example 1 Step 2, to afford the title compound (185 mg, 52%); ν_{max} (CH_2Cl_2) 3564, 3388, 2960, 2895, 1783, 1755, 1732, 1605, and 1478 cm^{-1}; ^1H NMR ($CDCl_3$) 0.74 (3H, d, *J* 6.8 Hz), 0.89 (3H, d, *J* 7.1 Hz), 1.0 - 1.3 (4H, m, including s at 1.19), 1.3 - 1.9 (12H, m, including s at 1.44), 2.0 - 2.4 (4H, m), 3.37 (1H, dd, *J* 6.6, 10.7 Hz; d, *J* 6.5 Hz after D_2O exch.), 4.47 (2H, s), 5.23 (1H, dd, *J* 1.4, 17.4 Hz), 5.38 (1H, dd, *J* 1.3, 10.9 Hz), 5.72 (1H, d, *J* 8.5 Hz), 6.47 (1H, dd, *J* 11.0, 17.4 Hz), 7.81 (1H, exch D_2O); MS(CI) *m/z* 457 (MNH_4^+).

Example 64. 19,20-Dihydromutilin 14-[*N*-(4-hydroxybenzoyl)]-carbamate

Mutilin 14-[*N*-(4-hydroxybenzoyl)]-carbamate (130 mg) in ethyl acetate (10 ml) containing 10% Pd-C catalyst (44 mg) and the mixture was hydrogenated at

atmospheric pressure for 30 min. The mixture was filtered through kieselguhr and the ethyl acetate was removed. chloroform / methanol was then added and removed and the chloroformwas added and removed to leave the title compound (131 mg) as a solid foam; ν_{max} (KBr) 1781, 1725, 1697, 1609, 1459, 1299, and 1201 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OD + D_2O) 0.7 - 1.27 (15H, m), 1.27 - 1.90 (10 H, m, including s at 1.46), 1.9 - 2.5 (5H, m), 3.39 (1h, d, *J* 5.4 Hz), 5.65 (1H, d, *J* 7.9 Hz), 6.84 (2H, d, *J* 8.7 Hz), 7.69 2H, d, *J* 8.7 Hz); MS(CI) *m/z* 486 (MH^+) 503 (MNH_4^+); MS(Electrospray) 503 (MNH_4^+) 544 (MNH_4^+ + MeCN).

Example 65. Mutilin 14-[*N*-(3-Amino-1,2,4-triazolylthioacetyl)]-carbamate

Mutilin 14-(*N*-Chloroacetyl)-carbamate (100 mg, 0.23 mmol) in *N,N*-dimethylformamide (2.5 ml) was treated with 3-amino-5-mercapto-1,2,4-triazole (29 mg, 0.25 mmol), followed by N,N-diisopropylethylamine (0.043 ml, 32 mg, 0.25 mmol). The mixture was stirred for 4.5 h and then ethyl acetate (25 ml) and water (15 ml) were added and the mixture was separated. The aqueous phase was re-extracted with ethyl acetate, and combined ethyl acetate layers were washed with brine, dried ($MgSO_4$) and evaporated. the residual oil was taken up in dichloromethane and loaded onto a silica gel column. Elution with ethyl acetate / hexane (1:1), followed by ethyl acetate, followed by ethyl acetate / ethanol gave the title compound, contaminated by a little DMF. The material was taken up in ethyl acetate and washed with water, followed by brine, dried ($MgSO_4$) and evaporated. Trituration of the residue with diethyl ether gave the title compound (102 mg, 85%); ^1H NMR ($CDCl_3$ + CD_3OD + D_2O) *inter alia* 0.63 (3H, d, *J* 6.4 Hz), 0.81 (3H, d, *J* 6.9 Hz), 0.9 - 1.8 (14H, m, including s at 1.04 and s at 1.32), 1.9 - 2.3 (5H, m), 3.65 and 3.72 (2H, ABq, *J* 15.2 Hz), 5.08 (1H, dd, *J* 1.4, 17.3 Hz), 5.22 (1H,dd, *J* 1.3, 11.1 Hz), 5.55 (1H, d, *J* 8.4 Hz), 6.35 (1H, dd, *J* 11.0, 17.4 Hz); MS(CI) 520 (MH^+).

Example 66. Mutilin 14-[*N*-(2-*N,N*-Diethylaminoethylthio-acetyl)]-carbamate

Mutilin 14-(*N*-Chloroacetyl)-carbamate (100 mg, 0.23 mmol) in tetrahydrofuran (2 ml) was treated with *N,N*-diethylaminoethane thiol hydrochloride (39 mg, 0.23 mmol) followed by 1M aqueous NaOH (0.5 ml). After stirring for 4.5 h ethyl acetate (25 ml) and water (20 ml) were added and the layers were separated. The aqueous layer was re-extracted with ethyl acetate and the combined extracts were washed ($MgSO_4$) and evaporated. the residue was chromatographed on silica gel,

eluting with CH_2Cl_2 / MeOH / 0.880 NH_4OH mixtures; 95:4.5:0.5, followed by 90:9:1 to give the title compound (20 mg); ^1H NMR ($CDCl_3$ + CD_3OD + D_2O) 0.73 (3H, d, *J* 6.4 Hz), 0.85 (3H, d, *J* 6.9 Hz), 1.00 (6H, t, *J* 7.1 Hz), 1.1 - 1.25 (4H, s superimposed on m), 1.25 - 1.9 (11H, m, including s at 1.42), 2.0 - 2.4 (6H, m), 2.53 (4H, q, *J* 7.1 Hz), 2.65 (4H, br. s), 3.33 (1H, d, *J* 6.3 Hz), 5.19 (1H, d, *J* 17.2 Hz), 5.33 (1H, d *J* 11.0 Hz), 5.70 (1H, d, *J* 8.3 Hz), 6.46 (1H, dd, *J* 11.0, 17.4 Hz).

Example 67. Mutilin 14-[*N*-(4-nitrobenzenesulphonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-nitrobenzenesulphonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (500 mg) in dry dichloromethane (10 ml) was treated with 4-nitrobenzenesulphonamide (508 mg), di*iso*propylethylamine (0.5 ml), and 4-dimethylaminopyridine (5 mg), and the solution was stirred for 2 hours at room temperature. The solution was diluted with ethyl acetate (100 ml) and washed with dilute HCl (100 ml), water (100 ml), and saturated brine (100 ml). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to yield the crude product as a colourless gum.

Step 2. Mutilin 14-[*N*-(4-nitrobenzenesulphonyl)]-carbamate

The crude (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-nitrobenzenesulphonyl)]-carbamate from Step1. was dissolved in 1,4-dioxane (12 ml) and treated with a saturated solution of zinc chloride in conc. HCl (4 ml). The solution was kept at room temperature for 4 hours, diluted with ethyl acetate (150 ml) and washed three times with water (100 ml portions). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to give a colourless gum. Chromatography on silica gel using ethyl acetate - hexane gave the title compound as a white solid (272 mg); ν_{max} (CH_2Cl_2) 3624, 3353, 1736, and 1608 cm^{-1}; δ_H ($CDCl_3$) 8.32 (2H, d, *J* 8.5 Hz), 8.18 (2H, d, *J* 8.5 Hz), 6.27 (1H, dd, *J* 17.5 and 11 Hz), 5.60 (1H, d, *J* 8.3 Hz), 5.22 (1H, d, *J* 11 Hz), 5.09 (1H, d, *J* 17.5 Hz), 3.30 (1H, dd, *J* 6.5 and 10 Hz), 2.22 (2H, m), 2.00 (2H, m), 1,8 - 1.0 (overlapping multiplets), 1.35 (3H, s), 1.09 (3H, s), 0.85 (3H, d, *J* 6.9 Hz), 0.51 (3H, d, *J* 6.7 Hz); MS (CI) *m/z* 566 ($M.NH_4^+$).

Example 68. Mutilin 14-[*N*-(4-cyanobenzenesulphonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-cyanobenzenesulphonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-chloroformate (400 mg) in dry dichloromethane (20 ml) was treated with 4-cyanobenzenesulphonamide (273 mg), di*iso*propylethylamine (0.4 ml), and 4-dimethylaminopyridine (4 mg), and the solution was stirred for 16 hours at room temperature. The solution was diluted with ethyl acetate (100 ml) and washed with dilute HCl (100 ml), water (100 ml), and saturated brine (100 ml). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to yield the crude product as a colourless gum.

Step 2. Mutilin 14-[*N*-(4-cyanobenzenesulphonyl)]-carbamate

The crude (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-cyanobenzenesulphonyl)]-carbamate from Step1. was dissolved in 1,4-dioxane (12 ml) and treated with a saturated solution of zinc chloride in conc. HCl (4 ml). The solution was kept at room temperature for 4 hours, diluted with ethyl acetate (150 ml) and washed three times with water (100 ml portions). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to give a colourless gum. Chromatography on silica gel using ethyl acetate - hexane gave the title compound as a white foam (185 mg); ν_{max} (CH_2Cl_2) 3627, 3348, and 1735 cm^{-1}; δ_H ($CDCl_3$) 8.12 (2H, d, *J* 8.5 Hz), 7.82 (2H, d, *J* 8.5 Hz), 6.27 (1H, dd, *J* 17.5 and 11 Hz), 5.60 (1H, d, *J* 8.4 Hz), 5.21 (1H, d, *J* 10.5 Hz), 5.10 (1H, d, *J* 17.5 Hz), 3.30 (1H, dd, *J* 6.5 and 10 Hz), 2.21 (2H, m), 2.00 (2H, m), 1,8 - 1.0 (overlapping multiplets), 1.33 (3H, s), 1.10 (3H, s), 0.86 (3H, d, *J* 6.9 Hz), 0.51 (3H, d, *J* 6.9 Hz); MS (CI) *m/z* 546 ($M.NH_4^+$).

Example 69. Mutilin 14-[*N*-(4-aminobenzenesulphonyl)]-carbamate

Mutilin 14-[*N*-(4-nitrobenzenesulphonyl)]-carbamate (265mg) was dissolved in ethanol (30ml) and ethyl acetate (5ml) and heated to gentle reflux with tin(II) chloride (458mg) for 5 hours under an atmosphere of argon. After cooling, the solvent was evaporated and the residue was chromatographed over silica gel, eluting with ethyl acetate - hexane mixtures. The title compound was obtained as a white solid (80mg); ν_{max} (CH_2Cl_2) 3407, 1735, 1624 and 1596 cm^{-1}; δ_H (d_6-

DMSO) 11.23 (1H, s, exchanges with D_2O), 7.44 (2H, d, *J* 8.8 Hz), 6.90 (1H, s, exchanges with D_2O), 6.59 (2H, d, *J* 8.8 Hz), 6.10 (1H, s, exchanges with D_2O), 6.10 (1H, dd, *J* 17.7 and 11.2 Hz), 5.32 (1H, d, *J* 7.6 Hz), 4.87 (1H, dd, *J* 11.2 and 1.4 Hz), 4.78 (1H, dd, *J* 17.8 and 1.4 Hz), 4.51 (1H, d, J 6.0 Hz, exchanges with D_2O), 3.30 (1H, d), 2.3-1.0 (overlapping multiplets), 1.30 (3H, s),0.98 (3H, s), 0.78 (3H, d, *J* 6.9 Hz), 0.48 (3H, d, *J* 6.3 Hz); MS (CI) *m/z* 536 ($M.NH_4^+$).

Example 70. Mutilin 14-[*N*-(6-Ethoxybenzothiazolyl-2-sulphonyl)]-carbamate

Step 1. 11-*O*-Dichloroacetyl-Mutilin 14-[*N*-(6-Ethoxybenzotriazolyl-2-sulphonyl)]-carbamate

A solution of mutilin 14-chloroformate-11-dichloroacetate (246mg, 0.5 mmol) in dichloromethane (1 ml) was added to an ice-cooled solution of 6-ethoxybenzothiazole-2-sulphonamide (130 mg, 0.5 mmol) and *N,N*-di-*iso*propylethylamine (0.092 ml, 1.05 eq) in dichloromethane (2 ml)-DMF (0.5 ml). The cooling bath was removed and the solution stirred at room temperature for 3 days. The solution was diluted with ethyl acetate and washed with dil. HCl , with water and with brine. Drying ($MgSO_4$) and evaporation gave a foam (ca 350 mg) which was chromatographed on silica gel, using 5% methanol-chloroform to give the product as a white solid (142 mg): ν_{max} ($CHCl_3$) 3500, 3368, 1734, 1740 (shoulder), 1601 cm^{-1}.

Step 2. Mutilin 14-[*N*-(6-Ethoxybenzothiazolyl-2-sulphonyl)]-carbamate

The product of Step 1 (130 mg, 0.18 mmol) was dissolved in methanol (2 ml) and 1N NaOH (0.18 ml) was added. After stirring for 1 hr a further portion of 1N NaOH (0.18 ml) was added. After a total of 3 hr the mixture was acidified by adding 2N HCl (0.2 ml) and extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$) and evaporated to give a gum (140 mg). Chromatography on silica gel, using 10% methanol-chloroform gave the title compound as a white solid (96 mg, 87%); ν_{max} ($CHCl_3$) 3370, 1737, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) 0.59 (3H, d, J 6.7), 0.82 (3H, d, J 6.9), 0.94 (3H, s), 0.9-1.1 (ca 12H, m), 1.25-1.7 (ca 15H, m) 1.8-2.25 (ca 4H, m), 3.24 (1H, dd, J 9, 7 collapse to d, J 6 with D_2O), 4.13 (2H, q, J 7), 5.00 (1H, d, J 17), 5.11 (1H, d, J 11), 5.62 (1H, d, J 8), 6.2 (1H, br, collapse to dd, J 17,11 with D_2O), 7.2 1H, dd J 2.2, 9), 7.35 (1H, d, J 2.3), 8.0 (1H, d, J 9); MS (NH_3DCI) m/z 605 (MH^+), 622 (MNH_4^+)

Example 71. Mutilin 14-[*N*-(2,4-Dimethylthiazolyl-5-sulphonyl)]-carbamate

Step 1. 11-*O*-Dichloroacetyl-Mutilin-14-[*N*-(2,4-Dimethylthiazolyl-5-sulphonyl)]-carbamate

A solution of mutilin 14-chloroformate-11-dichloroacetate (493mg, 1 mmol) in dichloromethane (4 ml) was added to an ice-cooled solution of 2,4-dimethylthiazole-5-sulphonamide (192 mg, 1 mmol) and *N,N*-di-*iso*propylethylamine (0.175 ml, 1 mmol) in dichloromethane (5 ml)-DMF (0.5 ml). The cooling bath was removed and the solution stirred at room temperature overnight, refluxed for 5hr and left again at room temperature overnight. Examination by tlc showed that reaction was almost complete. Evaporation of solvent followed by chromatography on silica gel, using 2% methanol-chloroform gave an impure product which was further chromatographed using 1:1 ethyl acetate-hexane. The product was obtained as a white solid (188 mg); ν_{max} ($CHCl_3$) 3378, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) inter alia 2.70 (3H, s), 4.89 (1H, d, J 7), 5.17 (1H, d, J 17), 5.24 (1H, d, J 11), 5.58 (1H, d, J 8), 5.98 (1H, s), 6.21(1H, dd J 17, 11), 7.5-7.8 (1H, br); MS (NH_3DCI) m/z 649/651 (MH^+).

Step 2. Mutilin 14-[*N*-(2,4-Dimethylthiazolyl-5-sulphonyl)]-carbamate

The product of Step 1 (175 mg, 0.27 mmol) was dissolved in methanol (5 ml)-tetrahydrofuran (2 ml) and 1N NaOH (0.50 ml; 1.85 eq) was added. After 3 hr at room temperature the mixture was acidified by adding 2N HCl (0.25 ml) and extracted with ethyl acetate (50 ml). The extract was washed with water and with brine, dried ($MgSO_4$)and evaporated to give a gum (140 mg). Chromatography on silica gel, using 1:1 ethyl acetate-hexane gave the title compound as a white foam (85 mg); ν_{max} ($CHCl_3$) 3694, 3562, 1736 cm^{-1}; ^1H NMR ($CDCl_3$) 0.61 (3H, d, J 6.8), 0.86 (3H, d, J 7), 1.1-1.8 (ca 15H, m), 2.0-2.25 (ca 5H, m), 2.64 (3H, s), 2.70 (3H, s), 3.32 (1H, d, J 6.5), 5.14 (1H, dd, J 17, 1.3), 5.30 (1H, dd, J 10, 1.3), 5.66 (1H, d, J 8), 6.32 (1H, dd, J 17,11), 7.71(1H, br, exch D_2O); MS (EI) m/z 538 (M^+). Found: 538.2171, $C_{26}H_{38}N_2O_6S_2$ requires 538.2172.

Example 72. Mutilin 14-[*N*-(Thiophene-2-sulphonyl)]-carbamate

Step 1. 11-*O*-Dichloroacetyl-Mutilin 14-[*N*-(Thiophene-2-sulphonyl)]-carbamate

A solution of mutilin 14-chloroformate-11-dichloroacetate (370 mg, 0.75 mmol) in dichloromethane (1 ml) was added to an ice-cooled solution of thipohene-2-

sulphonamide (122 mg, 0.75 mmol), *N,N*-di-*iso*propylethylamine (0.13 ml) and 4-dimethylaminopyridine (2mg) in dichloromethane (3 ml)-DMF (0.4 ml). The cooling bath was removed and the solution stirred at room temperature overnight. The solution was diluted with ethyl actetate and washed with dil. HCl and with brine. The solution was dried ($MgSO_4$) and evaporated to give a gum which was chromatographed on silica gel, using 5% acetone-toluene to give the product as a white foam (280 mg): ν_{max} ($CHCl_3$) 3381, 1736 cm^{-1}; ^1H NMR ($CDCl_3$) inter alia 4.88 (1H, d, J 6.9), 5.15 (1H, d, J 17), 5.24 (1H, d, J 11), 5.58 (1H, d, J 8), 5.97 (1H, s), 6.21 (1H, dd, J 17, 11), 7.12 (1H, dd, J 5, 3.8), 7.70 (1H, dd, J 5, 1.4), 7.85 (1H, dd, J 3.8, 1.4); MS (NH_3DCI) m/z 637/639 (MNH_4^+).

Step 2. Mutilin 14-[*N*-(Thiophene-2-sulphonyl)]-carbamate

The product from Step 1 (248 mg, 0.4 mmol) was dissolved in methanol (4 ml) and 1N NaOH (0.8 ml, 2 eq) was added. After 4 hr the mixture was acidified by adding 2N HCl and extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$) and evaporated to give a gum which was purified by chromatography on silica gel, using 1:1 ethyl acetate-hexane. The title compound was obtained as a white solid (155 mg); ν_{max} ($CHCl_3$) 3380, 1736 cm^{-1}; ^1H NMR ($CDCl_3$) 0.57 (3H, d, J 6.8), 0.85 (3H, d, J 7), 1.11 (3H, s), 1.38 (3H, s), 1.2-1.75 (ca 11H, m), 1.92-2.05 (2H, m), 2.22 (2H, q, J 8), 3.31 (1H, dd, J 10, 6.8), 5.12 (1H, dd J 17, 1.4), 5.28 (1H, dd, J 11, 1.4), 5.67 (1H, d, J 8.4), 7.11 (1H, dd, J 5, 4), 7.69 (1H, dd J 5, 1.2), 7.84 (1H, dd, J 4, 1.2), 7.5 (1H, br); MS (NH_3DCI) m/z 527 (MNH_4^+).

Example 73. Mutilin 14-[*N*-(5-Acetamido-1,3,4-thiadiazolyl-2-sulphonyl)]-carbamate

Step 1. 11-*O*-Dichloroacetyl-Mutilin 14-[*N*-(5-Acetamido-1,3,4-thiadiazolyl-2-sulphonyl)carbamate]

A solution of mutilin 14-chloroformate-11-dichloroacetate (246 mg, 0.5 mmol) in DMF (1 ml) was added to a solution of 5-acetamido-1,3,4-thiadiazole-2-sulphonamide (111 mg, 0.5 mmol), *N,N*-di-*iso*propylethylamine (0.09 ml, 1.05 eq) and 4-dimethylaminopyridine (cat.) in DMF (1 ml). The solution was stirred at room temperature overnight, diluted with ethyl actetate and washed with dil. HCl and with brine. The solution was dried ($MgSO_4$) and evaporated to give a gum which was chromatographed on silica gel, using 10% methanol-chloroform to give the product as a white solid (97 mg).

Step 2. Mutilin 14-[*N*-(5-Acetamido-1,3,4-thiadiazolyl-2-sulphonyl)]-carbamate

The product of Step 1 (95 mg) was dissolved in THF (0.5 ml) and methanol (1.5 ml). 1N NaOH (0.28 ml, 2 eq) was added and the solution left at room tempeature for ca 24 hr during which time a further portion of 1N NaOH (0.14 ml) was added. The solution was acidified with 2N HCl and extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$) and evaporated to give a gum which was purified by chromatography on silica gel, using 10% methanol-chloroform and rechromatographed using using ethyl acetate. The title compound was obtained as a white solid (19 mg, 24%); ^1H NMR (d_6-acetone-D_2O) inter alia 2.36 (3H, s), 3.54 (1H, d J 6), 5.0-5.1 (ca 2H, m), 5.58 (1H, d, J 8), 6.18 (1H, dd, J 17, 11); MS (Electrospray) m/z 569 (MH^+).

Example 74. Mutilin 14-[*N*-(3-amino-4-methoxybenzoyl)]-carbamate

Step 1. 4-Methoxy-3-nitrobenzoylisocyanate

Silver cyanate (967 mg, 6.5 mmol) was suspended in dry dichloromethane (6 ml) under an atmosphere of argon. A solution of 4-methoxy-3-nitrobenzoyl chloride (1.29 g, 6.0 mmol) in dichloromethane (4 ml) was added and the heterogeneous mixture stirred at reflux under subdued light. After 40 minutes the reaction was allowed to cool and filtered through Kieselguhr. The solution was used immediately in the next reaction. ν_{max} (CH_2Cl_2) 2337 cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-methoxy-3-nitrobenzoyl)]-carbamate

The solution from step 1 was cooled to 0°C and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500 mg, 1.5 mmol) and the reaction stirred for 1 hour. The mixture was diluted with dichloromethane and washed with 1.0M hydrochloric acid followed by water and saturated sodium chloride solution. After drying ($MgSO_4$) the crude material was purified by chromatography on silica gel eluting with 40% ethyl acetate in hexane to yield the title compound (770 mg, 92%); m.p. 178-180°C; ν_{max} (CH_2Cl_2) 3300, 2980, 1777, 1697, 1619 and 1476cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 0.99 (3H, d, *J* 6.4Hz), 1.07-1.58 (12H, m) including 1.21 (3H, s) and 1.31 (3H, s), 1.68-1.76 (2H, m), 1.94-2.04 (2H, m), 2.20 (1H, m), 2.54 (1H, dd, *J* 15.3, 10.0Hz), 2.90 (1H, q, *J* 6.2Hz), 3.24 (3H, s), 3.48 (1H, m), 4.05 (3H, s), 5.01 (1H, d, *J* 17.4Hz), 5.26 (1H, d, *J* 10.7Hz), 5.86 (1H, d, *J* 9.9Hz), 6.67 (1H, dd, *J*

17.4, 10.7Hz), 7.20 (1H, d, *J* 8.9Hz), 8.09 (1H, s), 8.12 (1H, dd, *J* 8.9, 2.4Hz); 8.33 (1H, d, *J* 2.4Hz); MS (Electrospray) *m/z* 574 (MNH_4^+); (Found: C, 64.33; H, 7.48; N, 4.68. $C_{30}H_{40}N_2O_8$ requires C, 64.73; H, 7.24; N, 5.03).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-amino-4-methoxybenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-methoxy-3-nitrobenzoyl)carbamate] (720 mg, 1.29 mmol) was suspended in ethanol (30 ml). Addition of ethyl acetate (6 ml) brought about complete dissolution. Tin (II) chloride (1.26 g, 6.65 mmol) was added and the reaction warmed to reflux whilst under an atmosphere of argon. After 3 hours the reaction was allowed to cool and poured into ethyl acetate and water before neutralising with sodium hydrogen carbonate. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 40% ethyl acetate in hexane. The title compound was isolated as a colourless foam (297 mg, 44%); ν_{max} (CH_2Cl_2) 3393, 2981, 1773, 1698, 1605 and 1474cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.6Hz), 0.99 (3H, d, *J* 6.4Hz), 1.05-1.55 (12H, m) including 1.21 (3H, s) and 1.34 (3H, s), 1.70-1.79 (2H, m), 1.94-2.08 (2H, m), 2.21 (1H, m), 2.53 (1H, dd, *J* 15.3, 10.0Hz), 2.92 (1H, q, *J* 6.1Hz), 3.26 (3H, s), 3.48 (1H, m), 3.93 (3H, s), 3.99 (2H, bs), 5.03 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.8Hz), 5.84 (1H, d, *J* 9.9Hz), 6.73 (1H, dd, *J* 17.5, 10.8Hz), 6.82 (1H, d, *J* 8.6Hz), 7.18 (1H, dd, *J* 8.6, 2.3Hz), 7.23 (1H, d, *J* 2.3Hz), 7.90 (1H, s); MS (Electrospray) *m/z* 527 (MH^+).

Step 4. Mutilin-14-[*N*-(3-amino-4-methoxybenzoyl)]-carbamate

The product of Step 3 (100 mg, 0.19 mmol) in dioxane (1 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml) and the reaction stirred at room for 30 minutes. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 70% ethyl acetate in hexane. The title compound was isolated as a colourless foam (53 mg, 54%); ν_{max} (CH_2Cl_2) 3393, 2939, 1774, 1733, 1615 and 1476cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.88 (3H, d, *J* 7.0Hz), 1.12-1.80 (16H, m) including 1.19 (3H,s) and 1.51 (3H, s), 2.08-2.40 (4H, m), 3.37 (1H, dd, *J* 11.0, 6.6Hz), 3.91 (3H, s), 3.93 (2H, bs), 5.22 (1H, dd, *J* 17.4, 1.4Hz), 5.39 (1H, dd, *J* 10.9, 1.4Hz), 5.81 (1H, d, *J* 8.5Hz), 6.59 (1H, dd, *J* 17.4, 10.9Hz), 6.89 (1H, d, *J* 8.4Hz), 7.11-7.20 (2H, m), 7.80 (1H, bs); MS (Electrospray) *m/z* 513 (MH^+).

Example 75. Mutilin 14-[*N*-(3-methanesulphonamido-4-methoxybenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-methanesulphonamido-4-methoxybenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-amino-4-methoxybenzoyl)carbamate] (158 mg, 0.30 mmol) was dissolved in dichloromethane (5 ml) and treated with pyridine (81 ul, 1.05 mmol) followed by methanesulphonyl chloride (81 ul, 1.05 mmol). After stirring for 3 hours, the reaction mixture was diluted with dichloromethane and washed successively with 0.5M hydrochloric acid, saturated aqueous sodium hydrogem carbonate, water and brine. The organic phase was dried over magnesium sulphate and concentrated *in vacuo*. The residue was purified by chromatography eluting with 70% ethyl acetate in hexane to yield a colourless foam (159 mg, 88%); ν_{max} (CH_2Cl_2) 3338, 2981, 1775, 1697, 1607 and 1476cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 1.02 (3H, d, *J* 6.4Hz), 1.05-1.59 (12H, m) including 1.20 (3H, s) and 1.31 (3H, s), 1.70-1.78 (2H, m), 1.96-2.07 (2H, m), 2.22 (1H, m), 2.55 (1H, dd, *J* 15.2, 10.1Hz), 2.91 (1H, q, *J* 6.4Hz), 3.02 (3H, s), 3.23 (3H, s), 3.48 (1H, m), 3.99 (3H, s), 5.01 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.8Hz), 5.83 (1H, d, *J* 9.9Hz), 6.72 (1H, dd, *J* 17.5, 10.8Hz), 6.86 (1H, bs), 7.02 (1H, d, *J* 8.6Hz), 7.72 (1H, dd, *J* 8.6, 2.2Hz), 7.93 (1H, d, *J* 2.2Hz), 7.99 (1H, s).

Step 2. Mutilin-14-[*N*-(3-methanesulphonamido-4-methoxybenzoyl)]-carbamate

The product of Step 1 (128 mg, 0.21 mmol) in dioxane (1 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml) and the reaction stirred at room for 30 minutes. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 70% ethyl acetate in hexane. The title compound was isolated as a colourless foam (46 mg, 37%); ν_{max} (CH_2Cl_2) 3340, 2941, 1776, 1733, 1607 and 1477cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.81 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 6.9Hz), 1.10-1.82 (16H, m) including 1.21 (3H, s) and 1.52 (3H, s), 2.10-2.38 (4H, m), 2.99 (3H, s), 3.38 (1H, dd, *J* 10.8, 6.5Hz), 3.96 (3H, s), 5.22 (1H, dd, *J* 17.4, 1.4Hz), 5.38 (1H, dd, *J* 11.1, 1.4Hz), 5.82 (1H, d, *J* 8.4Hz), 6.54 (1H, dd, *J* 17.4, 11.1Hz), 6.84 (1H, bs), 6.99 (1H, d, *J* 8.6Hz), 7.70 (1H, dd, *J* 8.6, 2.3Hz), 7.88 (1H, d, *J* 2.3Hz), 7.95 (1H, bs).

Example 76. Mutilin 14-[*N*-(isoxaxol-5-oyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(isoxazol-5-oyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (633 mg, 1.89 mmol) was combined with isoxazole-5-carbonyl chloride (1.0g, 7.60 mmol), silver cyanate (1.22 g, 8.14 mmol) and tetrakis(triphenylphosphine) palladium (0) (32 mg) in dry dichloromethane (15 ml) and the reaction stirred at room temperature for 30 minutes in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 30% ethyl acetate in hexane. The title compound was isolated as a colourless foam (850 mg, 95%); ν_{max} (CH_2Cl_2) 3393, 2929, 1783, 1726, 1597 and 1496cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.88 (3H, d, *J* 6.8Hz), 1.01 (3H, d, *J* 6.4Hz), 1.08-1.59 (12H, m) including 1.20 (3H, s) and 1.31 (3H, s), 1.69-1.77 (2H, m), 1.93-2.07 (2H, m), 2.21 (1H, m), 2.56 (1H, dd, *J* 15.3, 10.1Hz), 2.89 (1H, q, *J* 6.3Hz), 3.22 (3H, s), 3.48 (1H, m), 5.02 (1H, d, *J* 17.5Hz), 5.31 (1H, d, *J* 10.7Hz), 5.86 (1H, d, *J* 10.0Hz), 6.68 (1H, dd, *J* 17.5, 10.7Hz), 7.03 (1H, d, *J* 1.8Hz), 8.39 (1H, bs), 8.43 (1H, d, *J* 1.8Hz); MS(CI) *m/z* 490 (MNH_4^+).

Step 2. Mutilin-14-[*N*-(isoxazol-5-oyl)]-carbamate

The product of Step 1 (810 mg, 1.71 mmol) in dioxane (6 ml) was treated with a saturated solution of zinc chloride in conc. HCl (3 ml) and the reaction stirred at room for 30 minutes. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane to yield the title compound (540 mg, 69%); ν_{max} (CH_2Cl_2) 3395, 2959, 1785, 1731 and 1496cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.8Hz), 0.90 (3H, d, *J* 7.0Hz), 1.10-1.83 (16H, m) including 1.20 (3H, s) and 1.50 (3H, s), 2.10-2.37 (4H, m), 3.38 (1H, dd, *J* 10.8, 6.6Hz), 5.23 (1H, dd, *J* 17.3, 1.4Hz), 5.40 (1H, dd, *J* 10.9, 1.4Hz), 5.85 (1H, d, *J* 8.5Hz), 6.53 (1H, dd, *J* 17.3, 10.9Hz), 7.10 (1H, d, *J* 1.9Hz), 8.36 (1H, bs), 8.41 (1H, d, *J* 1.9Hz); MS(CI) *m/z* 476 (MNH_4^+).

Example 77. Mutilin 14-[*N*-(methoxyacetyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(methoxyacetyl)]-carbamate

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500 mg, 1.50 mmol) was combined with methoxyacetyl chloride (547 ul, 6.0 mmol) and silver cyanate (965 mg, 6.40 mmol) in dry dichloromethane (15 ml) and the reaction stirred at room temperature for 10 minutes in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 30% ethyl acetate in hexane. The title compound was isolated as a colourless foam (630 mg, 94%); ν_{max} (CH_2Cl_2) 3388, 2932, 1786, 1722 and 1488cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.85 (3H, d, *J* 6.9Hz), 1.00 (3H, d, *J* 6.4Hz), 1.08-1.58 (12H, m) including 1.19 (3H, s) and 1.28 (3H, s), 1.64-1.77 (2H, m), 1.94-2.06 (2H, m), 2.21 (1H, m), 2.51 (1H, dd, *J* 15.3, 10.1Hz), 2.88 (1H, q, *J* 6.4Hz), 3.21 (3H, s), 3.42 (1H, m), 3.49 (3H, s), 4.08 (2H, s), 5.01 (1H, d, *J* 17.6Hz), 5.30 (1H, d, *J* 10.7Hz), 5.77 (1H, d, *J* 10.0Hz), 6.69 (1H, dd, *J* 17.6, 10.7Hz), 8.26 (1H, bs).

Step 2. Mutilin-14-[*N*-(methoxyacetyl)]-carbamate

The product of Step 1 (600 mg, 1.34 mmol) in dioxane (6 ml) was treated with a saturated solution of zinc chloride in conc. HCl (3 ml) and the reaction stirred at room for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 40% ethyl acetate in hexane to yield the title compound as a colourless foam (210 mg, 36%); ν_{max} (CH_2Cl_2) 3388, 2941, 1787, 1726 and 1488cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.74 (3H, d, *J* 6.7Hz), 0.90 (3H, d, *J* 7.0Hz), 1.10-1.85 (16H, m) including 1.17 (3H, s) and 1.48 (3H, s), 2.04-2.37 (4H, m), 3.35 (1H, dd, *J* 10.9, 6.6Hz), 3.45 (3H, s), 4.06 (2H, s), 5.22 (1H, dd, *J* 17.4, 1.5Hz), 5.38 (1H, dd, *J* 11.0, 1.5Hz), 5.75 (1H, d, *J* 8.5Hz), 6.52 (1H, dd, *J* 17.4, 11.0Hz), 8.20 (1H, bs); MS(CI) *m/z* 453 (MNH_4^+).

Example 78. Mutilin 14-[*N*-(6-methoxynicotinoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(6-methoxynicotinoyl)carbamate]

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500 mg, 1.50 mmol) was combined with 6-methoxynicotinoyl chloride (430 mg, 2.5 mmol) and silver cyanate (400 mg, 2.67 mmol) in dry dichloromethane (20 ml) and the reaction stirred at room temperature for 4.5 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 30% ethyl acetate in hexane. The title compound was isolated as a colourless foam (750 mg, 98%); ν_{max} (CH_2Cl_2) 3423, 2930, 1776, 1729, 1603 and 1477cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.91 (3H, d, *J* 6.8Hz), 1.01 (3H, d, *J* 6.4Hz), 1.10-1.59 (12H, m) including 1.27 (3H, s) and 1.36 (3H, s), 1.68-1.78 (2H, m), 1.96-2.04 (2H, m), 2.21 (1H, m), 2.52 (1H, dd, *J* 15.3, 10.1Hz), 2.91 (1H, q, *J* 6.4Hz), 3.23 (3H, s), 3.49 (1H, m), 4.02 (3H, s), 5.03 (1H, d, *J* 17.4Hz), 5.30 (1H, d, *J* 10.8Hz), 5.84 (1H, d, *J* 10.0Hz), 6.69 (1H, dd, *J* 17.4, 10.8Hz), 6.83 (1H, d, *J* 8.8Hz), 7.91 (1H, bs), 8.05 (1H, dd, *J* 8.8, 2.6Hz), 8.63 (1H, d, *J* 2.6Hz); MS(CI) *m/z* 513 (MH^+).

Step 2. Mutilin-14-[*N*-(6-methoxynicotinoyl)]-carbamate

The product of Step 1 (720 mg, 1.41 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (3 ml) and the reaction stirred at room for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane to yield the title compound as a colourless foam (600 mg, 85%); ν_{max} (CH_2Cl_2) 3423, 2949, 1777, 1733, 1603 and 1475cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.82 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 7.0Hz), 1.10-1.82 (16H, m) including 1.20 (3H, s) and 1.49 (3H, s), 2.06-2.37 (4H, m), 3.36 (1H, dd, *J* 10.9, 6.5Hz), 3.99 (3H, s), 5.24 (1H, dd, *J* 17.4, 1.4Hz), 5.39 (1H, dd, *J* 11.0, 1.4Hz), 5.82 (1H, d, *J* 8.5Hz), 6.54 (1H, dd, *J* 17.4, 11.0Hz), 6.81 (1H, d, *J* 8.8Hz), 7.92 (1H, bs), 8.01 (1H, dd, *J* 8.8, 2.5Hz), 8.62 (1H, d, *J* 2.5Hz); MS(CI) *m/z* 499 (MH^+).

Example 79. Mutilin 14-[*N*-(pyrazin-2-oyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(pyrazin-2-oyl)carbamate]

(3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500 mg, 1.50 mmol) was combined with pyrazin-2-oyl chloride (1.14 g, 8.0 mmol) and silver cyanate (1.20 g, 8.0 mmol) in dry dichloromethane (15 ml) and the reaction stirred at room temperature for 10 minutes in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 40% ethyl acetate in hexane. The title compound was isolated as a colourless foam (498 mg, 69%); ν_{max} (CH_2Cl_2) 3364, 2931, 1781, 1720, 1697 and 1490cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.8Hz), 1.01 (3H, d, *J* 6.4Hz), 1.09-1.61 (12H, m) including 1.20 (3H, s) and 1.38 (3H, s), 1.69-1.79 (2H, m), 1.94-2.06 (2H, m), 2.21 (1H, m), 2.56 (1H, dd, *J* 15.3, 10.1Hz), 2.92 (1H, q, *J* 6.4Hz), 3.24 (3H, s), 3.50 (1H, m), 5.03 (1H, d, *J* 17.4Hz), 5.32 (1H, d, *J* 10.7Hz), 5.89 (1H, d, *J* 9.9Hz), 6.75 (1H, dd, *J* 17.4, 10.7Hz), 8.62 (1H, d, *J* 2.5Hz), 8.88 (1H, d, *J* 2.5Hz), 9.51 (1H, d, *J* 1.5Hz), 9.76 (1H, bs).

Step 2. Mutilin-14-[*N*-(pyrazin-2-oyl)]-carbamate

The product of Step 1 (450 mg, 0.93 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room for 1 hour. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane to yield the title compound as a colourless foam (420 mg, 96%); ν_{max} (CH_2Cl_2) 3364, 2939, 1782, 1734 and 1491cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.7Hz), 0.91 (3H, d, *J* 7.0Hz), 1.10-1.85 (16H, m) including 1.20 (3H, s) and 1.58 (3H, s), 2.10-2.43 (4H, m), 3.39 (1H, dd, *J* 10.9, 6.6Hz), 5.24 (1H, dd, *J* 17.4, 1.5Hz), 5.40 (1H, dd, *J* 10.9, 1.4Hz), 5.85 (1H, d, *J* 8.5Hz), 6.59 (1H, dd, *J* 17.4, 10.9Hz), 8.60 (1H, d, *J* 2.3Hz), 8.84 (1H, d, *J* 2.5Hz), 9.45 (1H, d, *J* 2.3Hz), 9.72 (1H, bs); MS(CI) *m/z* 487 (MNH_4^+).

Example 80. Mutilin 14-(*N*-thiophen-2-oyl)-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-thiophen-2-oyl)-carbamate

A suspension of silver cyanate in dichloromethane (10ml) was treated with 2-thiophene carbonyl chloride and the mixture heated under reflux for 45mins. IR analysis showed no starting material. The reaction mixture was cooled and filtered through Kieselguhr affording a pale yellow solution. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.5 g) was added to the solution. After 20mins. the solution was washed with dilute hydrochloric acid, saturated sodium chloride and then dried over anhydrous magnesium sulphate. Removal of solvent *in vacuo* afforded the product as a white solid which was purified by silica gel chromatography eluting with dichloromethane then 1% and 2% acetone/ dichloromethane to give the title compound as a white solid (0.686g, 94%); ν_{max} (CH_2Cl_2) 3422, 1773, 1726(w), 1698, 1521 and 1481 cm^{-1}; ^1H NMR ($CDCl_3$) 0.89 (3H, d, J6.8Hz), 1.01 (3H, d, J6.4Hz), 1.07-1.78 (8H, m), 1.20 (3H, s), 1.34 (3H, s), 1.99 (2H, m), 2.21 (1H,m), 2.55 (1H, dd, J10.1,15.3Hz), 2.90 (1H, q, J6.4Hz), 3.22 (3H, s), 3.46 (1H, m), 5.01 (1H, d, J17.5), 5.28 (1H, d, J10.7Hz), 5.86 (1H, d, J10.0Hz), 6.70 (1H, d, J10.7,17.5Hz), 7.13 (1H, m), 7.66 (2H, m) and 8.03 (1H, s); MS (NH_3 DCI) *m/z* 488 (MH^+) and 505 (MNH_4^+).

Step 2. Mutilin 14-(*N*-thiophen-2-oyl)-carbamate

The product from Step 1 (0.45 g) in dioxan (1.5 ml) was treated with Lukas reagent (sat. $ZnCl_2$/conc. HCl; 1.5 ml), at room temperature. The reaction mixture darkened and became warm. After 5 min. t.l.c. analysis showed no starting material. The reaction mixture was diluted with ethyl acetate and the solution washed with water. The organic phase was extracted with ethyl acetate and the combined organic extracts washed with saturated sodium hydrogen carbonate, saturated sodium chloride, dried and concentrated to an orange gum. Silica gel chromatography eluting with ethyl acetate/ hexane gave the product as a white solid, (0.173g, 40%); ν_{max} (CH_2Cl_2) 3564, 3424, 1775, 1733, 1705, 1521 and 1482 cm^{-1}; ^1H NMR ($CDCl_3$) 0.80 (3H, d, J6.7Hz), 0.89 (3H, d, 7.0Hz), 1.14 (1H, m), 1.19 (3H, s), 1.37-1.82 (9H, m), 1.54 (3H, s), 2.12-2.37 (4H, m), 3.37 (1H, dd, J6.6,10.6Hz), 5.23 (1h, dd, J1.5,17.4Hz), 5.36 (1H, dd, J1.5,11.1Hz), 5.83 (1H, d, J8.5Hz), 6.54 (1H, J, 11.0,17.4Hz), 7.12 (1H, m), 7.63 (2H, m) and 7.95 (1H, s); MS (NH_3 DCI) *m/z* 474 (MH^+) and 491 (MNH_4^+).

Example 81. Mutilin 14-[(S)-Tetrahydrofuran-2-oyl]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[(S)-tetrahydrofuran-2-oyl]-carbamate

(S)-(-)-Tetrahydrofuroic acid (0.464 g) in dichloromethane (3 ml) at room temperature was treated with oxalyl chloride (0.635 g) and one drop of DMF for 1 h. IR analysis showed complete conversion to the acid chloride. The solvent and excess oxalyl chloride were removed *in vacuo* and the residue redissolved in dry dichloromethane.

The acid chloride was reacted with silver cyanate (0.645 g) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.322 g) as previously described in Example 80, Step 1. Following purification by silica gel chromatography the product was isolated as a colourless foam, (0.43 g, 91%); ν_{max} (CH_2Cl_2) 3381, 1783, 1744, 1717 and 1698 cm^{-1}; ^1H NMR ($CDCl_3$) 0.83 (3H, d, J6.9Hz), 0.99 (3H, d, J6.4Hz), 1.06-1.75 (9H, m), 1.19 (3H, s), 1.29 (3H, s), 1.87-2.38 (7H, m), 2.50 (1H, dd, J10.1,15.3Hz), 2.88 (1H, q, J6.4Hz), 3.22 (3H, s), 3.46 (1H, m), 3.96 (2H, m), 4.43 (1H, dd, J5.7,8.4Hz), 5.00 (1H, d, J17.4Hz), 5.29 (1H, d, J10.7Hz), 6.71 (1H, dd, J10.7,17.5Hz) and 8.59 (1H, s); MS (NH_4 DCI) *m/z* 494 (MNH_4^+).

Step 2. Mutilin 14-[(S)-tetrahydrofuran-2-oyl]-carbamate

The product from Step 1, (0.388 g) in dioxan (1 ml) was treated with Lukas reagent as described in Example 80, Step 2. After purification by silica gel chromatography the product was isolated as a colourless foam, (0.242 g, 64%); ν_{max} (CH_2Cl_2) 3562, 3381, 1784, 1733 and 1480 cm^{-1}; ^1H NMR ($CDCl_3$) 0.75 (3H, d, J6.7Hz), 0.89 (3H, d, J7.1Hz), 1.15 (1H, m), 1.18 (3H, s), 1.42-2.35 (19H, m), 1.50 (3H, s), 3.36 (1H, dd, J6.7,10.9Hz), 3.94 (2H, m), 4.40 (1H, dd, J5.8,8.4Hz), 5.22 (1H, dd, J1.5,17.4Hz), 5.37 (1H, dd, J1.5,10.9Hz), 5.77 (1H, d, J8.5Hz), 6.54 (1H, dd, J11.0,17.4Hz) and 8.51 (1H, s); MS (NH_4 DCI) *m/z* 479 (MNH_4^+).

Example 82. Mutilin 14-[(R)-Tetrahydrofuran-2-oyl]carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[(R)-tetrahydrofuran-2-oylcarbamate]

(R)-(+)-Tetrahydrofuroic acid (0.464 g) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.322 g) were converted into the title compound as

described in Example 80, Step 1. Following purification by silica gel chromatography the title compound was obtained as a colourless foam (0.432 g, 91%); ν_{max} (CH_2Cl_2) 3383, 1782, 1718, 1698 and 1474 cm^{-1}; ^1H NMR ($CDCl_3$) 0.86 (3H, d, J6.9Hz), 1.00 (3H, d, J6.4Hz), 1.06-1.75 (9H, m), 1.17 (3H, s), 1.28 (3H, s), 1.87-2.38 (7H, m), 2.50 (1H, dd, J10.1,15.3Hz), 2.88 (1H, q, J6.4Hz), 3.22 (3H, s), 3.46 (1H, m), 3.88-4.06 (2H, m), 4.43 (1H, dd, J5.7,8.4Hz), 5.00 (1H, d, J17.4Hz), 5.29 (1H, d, J10.7Hz), 6.71 (1H, dd, J10.7,17.5Hz) and 8.59 (1H, s); MS (NH_3 DCI) *m/z* 494 (MNH_4^+).

Step 2. Mutilin 14-[(R)-tetrahydrofuran-2-oyl]-carbamate

The product from Step 1 (0.38 g) in dioxan (1 ml) was treated with Lukas reagent as described in Example 80, Step 2. After purification by silica gel chromatography the product was isolated as a colourless foam (0.195 g, 53%); ν_{max} (CH_2Cl_2) 3560, 3382, 1783, 1733 and 1480 cm^{-1} ; ^1H NMR ($CDCl_3$) 0.76 (3H, d, J6.7Hz), 0.88 (3H, d, J7.1Hz), 1.15 (1H, m), 1.18 (3H, s), 1.42-2.35 (19H, m), 1.48 (3H, s), 3.36 (1H, dd, J6.7,10.9Hz), 3.86-4.05 (2H, m), 4.40 (1H, dd, J5.8,8.4Hz), 5.22 (1H, dd, J1.5,17.4Hz), 5.37 (1H, dd, J1.5,10.9Hz), 5.77 (1H, d, J8.5Hz), 6.54 (1H, dd, J11.0,17.4Hz) and 8.51 (1H, s); MS (NH_4 DCI) *m/z* 479 (MNH_4^+).

Example 83. Mutilin 14-[*N*-(2,4-Difluorobenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2,4-difluorobenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (200 mg), 2,4-difluorobenzoyl chloride (212 mg), and silver cyanate (180 mg) in dichloromethane (5 ml) were stirred at room temperature for 2 hours. The mixture was diluted with ethyl acetate (100 ml) and filtered. The filtrate was washed with water (2 x 30 ml) and saturated sodium bicarbonate solution (30 ml), the solution was dried (sodium sulphate), and the solvent was evaporated under reduced pressure to give the title compound as a colourless gum (400 mg); ^1H NMR ($CDCl_3$) *inter alia* 3.23 (3H, s), 3.46 (1H, m), 5.00 (1H, d, *J* 17.5 Hz), 5.30 (1H, d, *J* 10.5 Hz), 5.81 (1H, d, *J* 10 Hz), 6.72 (1H, dd, *J* 17.5, 10.5 Hz), 6.90 (1H, m), 7.03 (1H, m), 8.10 (1H, m), 8.40 (1H, d, *J* 13 Hz).

Step 2. Mutilin 14-[*N*-(2,4-Difluorobenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2,4-difluorobenzoyl)]-carbamate from Step 1 (400 mg) in 1,4-dioxane (5 ml) was treated with

a saturated solution of zinc chloride in conc. HCl (2 ml) and the solution was kept at room temperature for 3 hours. The solution was diluted with ethyl acetate (50 ml) and washed with water (2 x 30 ml) and saturated sodium bicarbonate solution (30 ml). The solution was dried (sodium sulphate) and the solvent was evaporated under reduced pressure to give a pale yellow gum. The gum was chromatographed on silica gel using gradient elution from 1:4 to 2:3 ethyl acetate/ hexane, to give the title compound as a white foam. Crystallisation from dichloromethane/ hexane gave colourless crystals (250 mg), m.p. 178 - 180°C; ^{1}H NMR ($CDCl_3$) *inter alia* 3.37 (1H, dd, *J* 11, 6.6 Hz), 5.23 (1H, dd, *J* 17.3, 1.4 Hz), 5.38 (1H, dd, *J* 11, 1.4 Hz), 5.80 (1H, d, *J* 8.5 Hz), 6.55 (1H, dd, *J* 17.3, 11 Hz), 6.91 (1H, m), 7.03 (1H, m), 8.10 (1H, m), 8.30 (1H, d, *J* 13 Hz).

Example 84. Mutilin 14-[*N*-(3,4-Difluorobenzoyl)]-carbamate

Using the methods described in Example 83, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (250 mg) and 3,4-difluorobenzoyl chloride (210 mg) were converted into (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3,4-difluorobenzoyl)]-carbamate [MS(EI) *m/z* 517 (M^+)], and hence into the title compound, which was obtained as colourless crystals (120 mg), m.p. 144 - 146 °C (dichloromethane/ hexane); ^{1}H NMR ($CDCl_3$) *inter alia* 3.37 (1H, dd, *J* 10.7, 6.6 Hz), 5.23 (1H, dd, *J* 17.3, 1.4 Hz), 5.32 (1H, dd, *J* 11, 1.3 Hz), 5.82 (1H, d, *J* 8.5 Hz), 6.50 (1H, dd, *J* 17.3, 11 Hz), 7.30 (1H, m), 7.60 (1H, m), 7.70 (1H, m), 8.13 (1H, s).

Example 85. Mutilin 14-[*N*-(1-*tert*-butyloxycarbonyl-azetidin-3-oyl)]-carbamate

Step 1. 1-*tert*-Butyloxycarbonyl-azetidine-3-carboxylic acid

3-Azetidine carboxylic acid (250 mg) in water (2 ml) was treated with a solution of di-*tert*-butyl dicarbonate (650 mg) in 1,4-dioxane (3 ml) and the mixture was stirred at room temperature for 17 hours. The mixture was acidified by adding a few drops of 1*M* HCl, was diluted with water (10 ml), and extracted with ethyl acetate (2 x 20 ml). The organic extract was washed with water (2 x 10 ml). The solution was dried (sodium sulphate) and the solvent was evaporated under reduced pressure to give a colourless gum. Crystallisation from diethyl ether/ pentane gave the title compound as colourless crystals (470 mg), m.p. 102.5 - 104 °C; ^{1}H NMR ($CDCl_3$) 1.44 (9H, s), 3.38 (1H, quin, *J* 7.4 Hz), 4.13 (4H, d, *J* 7.4 Hz).

Step 2. Mutilin 11-trifluoroacetate

Mutilin (960 mg) in dry tetrahydrofuran (12 ml) was treated with pyridine (0.3 ml) and the solution was cooled to 0°C. Trifluoroacetic anhydride (0.48 ml) was added dropwise over 3 minutes to the stirred solution. The solution was kept at 0°C for 2 hours, and was then diluted with ethyl acetate (100 ml) and washed with water (2 x 30 ml), sodium bicarbonate solution (30 ml), and saturated sodium chloride solution (30 ml). The solution was dried (sodium sulphate) and the solvent was evaporated under reduced pressure to give a colourless gum. The gum was chromatographed on silca gel using 1:9 to 1:4 ethyl acetate/ hexane to give the title compound as colourless crystals (570 mg). Recrystallisation from dichloromethane/ hexane gave colourless rods, m.p. 170 - 171 °C; ν_{max} ($CHCl_3$) 3636, 1777, and 1736 cm^{-1}; MS(EI) *m/z* 416 (M^+).

Step 3. Mutilin 14-[*N*-(1-*tert*-butyloxycarbonyl-azetidin-3-oyl)]-carbamate 11-trifluoroacetate

1-*tert*-Butyloxycarbonyl-azetidine-3-carboxylic acid (345 mg) in dry dichloromethane (10 ml) was treated with oxalyl chloride (254 mg; 0.175 ml) and *N*,*N*-dimethylformamide (1 drop). The solution was stirred for 1.5 hours, and then the solvent was removed by evaporation under reduced pressure. The residue was dissolved in toluene (10 ml), and the toluene was evaporation under reduced pressure to give 1-*tert*-butyloxycarbonyl-azetidine-3-carbonyl chloride as a colourless oil.

The oil was dissolved in dichloromethane (6 ml) and the solution was treated with silver cyanate (525 mg). The mixture was stirred for 10 minutes, and then mutilin 11-trifluoroacetate (535 mg) in dichloromethane (9 ml) was added. The mixture was stirred for 20 hours. Ethyl acetate (50 ml) was added and the mixture was filtered. The filtrate was washed with saturated sodium bicarbonate solution (20 ml) and saturated sodium chloride solution (20 ml). The solution was dried (sodium sulphate) and the solvent was removed under reduced pressure to yield a colourless gum. The gum was chromatographed on silica gel using 1:4 to 1:2 ethyl acetate/ hexane to give the title compound as a colourless gum (485 mg); ^1H NMR ($CDCl_3$) *inter alia* 1.43 (9H, s), 3.93 (1H, quin, *J* 7.2 Hz), 4.98 (1H, d, *J* 6.9 Hz), 4.14 (4H, m), 5.23 (1H, d, *J* 17.5 Hz), 5.29 (1H, d, *J* 11.2 Hz), 5.58 (1H, d, *J* 8 Hz), 6.31 (1H, dd, *J* 17.5, 11.2 Hz), 7.57 (1H, s).

Step 4. Mutilin 14-[*N*-(1-*tert*-butyloxycarbonyl-azetidin-3-oyl)]-carbamate

Mutilin 14-[*N*-(1-*tert*-butyloxycarbonyl-azetidin-3-oyl)]-carbamate 11-trifluoroacetate (450 mg) was dissolved in tetrahydrofuran (10 ml)/ water (2 ml)

and the solution was treated with 0.5*M* sodium hydroxide (1.5 ml). The mixture was stirred for 4.5 hours, and was then diluted with ethyl acetate (50 ml) and washed with water (2 x 30 ml). The solution was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to give the title compound as a white foam (380 mg); ν_{max} ($CHCl_3$) 3551, 3396, and 1706 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 1.43 (9H, s), 3.35 (1H, m), 3.94 (1H, quin, *J* 7.5 Hz), 4.10 (4H, m), 5.22 (1H, d, *J* 17.3 Hz), 5.35 (1H, d, *J* 11 Hz), 5.65 (1H, d, *J* 8.4 Hz), 6.42 (1H, dd, *J* 17.3, 11 Hz), 7.26 (1H,s).

Example 86. Mutilin 14-(*N*-azetidin-3-oyl)-carbamate

Mutilin 14-[*N*-(1-*tert*-butyloxycarbonyl-azetidin-3-oyl)]-carbamate (350 mg) in dichloromethane (8 ml) was treated with trifluoroacetic acid (0.5 ml) and the solution was kept at room temperature for 5 hours. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate (20 ml). The solution was extracted with dilute HCl (10 ml), and the extract was washed with ethyl acetate (10 ml). The aqueous solution was basified (pH 10) using potassium carbonate, and was then extracted with ethyl acetate (3 x 10 ml). The organic extract was washed with saturated sodium chloride and dried (sodium sulphate). The solvent was removed under reduced pressure to give a white waxy solid (125 mg). The solid was chromatographed on silca gel using 1:9:90 ammonia solution (35%)/ methanol/ dichloromethane to give the title compound as a white foam (100 mg); ^1H NMR (1:9 CD_3OD:$CDCl_3$) *inter alia* 3.33 (1H, d, *J* 6.3 Hz), 4.01 (4H, m), 5.20 (1H, d, *J* 17.4 Hz), 5.32 (1H, d, *J* 11.2 Hz), 5.64 (1H, d, *J* 8.3 Hz), 6.41 (1H, dd, *J* 17.4, 11.2 Hz); MS(ES) *m/z* 447 (MH^+).

Example 87. Mutilin 14-[*N*-(1-ethyl-piperidin-4-oyl)]-carbamate

Step 1. Ethyl 1-ethyl-isonipecotate

Ethyl isonipecotate (6.28 g) in ethanol (35 ml) was treated with ethyl iodide (6.86 g) and powdered potassium carbonate (10 g). The mixture was stirred and heated under reflux for 20 hours. The mixture was cooled to room temperature and the solid was removed by filtration and was washed with ethanol (2 x 10 ml). The ethanol was removed from the filtrate by evaporation under reduced pressure, and the resulting residue was partitioned between chloroform (100 ml) and water (50 ml). The organic layer was separated, washed with saturated sodium chloride solution, and dried (sodium sulphate). The solvent was removed by evaporation

under reduced pressure to give the title compound as a yellow oil (6.62 g); MS(EI) *m/z* 185 (M^+).

Step 2. 1-Ethyl-isonipecotic acid hydrochloride

Ethyl 1-ethyl-isonipecotate (5.5 g) was dissolved in water (22 ml)/ c.HCl (39 ml) and the solution was heated under reflux for 4 hours. The solvent was removed by evaporation under reduced pressure. The residue was dissolved in water (30 ml), and the water was removed by evaporation under reduced pressure. The residue was triturated with toluene (50 ml), and the toluene was removed by evaporation under reduced pressure to give a solid which was dried *in vacuo* for 18 hours. The title compound was thus obtained as a white powder (5.4 g); MS(EI) *m/z* 157 (M^+).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-ethyl-piperidin-4-oyl)]-carbamate

1-Ethyl-isonipecotic acid hydrochloride (0.95 g) was suspended in thionyl chloride (8 ml) and the mixture was stirred and heated under reflux for 3 hours to give a clear yellow solution. The thionyl chloride was removed by evaporation under reduced pressure and the resulting residue was suspended in toluene (5 ml) and the toluene was removed by evaporation under reduced pressure to give 1-ethyl-isonipecotoyl chloride hydrochloride as a white solid.
The acid chloride was suspended in dry dichloromethane (20 ml) and silver cyanate (1.5 g) was added. The mixture was stirred and heated under reflux for 1 hour. The mixture was cooled to room temperature and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1 g) and triethylamine (0.5 g) were added. The mixture was stirred at room temperature for 16 hours. The mixture was diluted with ethyl acetate (50 ml) and the solid was removed by filtration. The filtrate was washed with saturated sodium bicarbonate and saturated sodium chloride. The solution was dried (sodium sulphate), and the solvent was removed by evaporation under reduced pressure to give a yellow gum. The gum was chromatographed on silica gel using 1:3 ethyl acetate/ chloroform and 1:9:90 ammonia solution (35%)/ methanol/ dichloromethane to give the title compound as a colourless gum (134 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 2.88 (2H, q, *J* 6.5 Hz), 3.08 (3H, m), 3.22 (3H, s), 3.42 (1H, m), 5.04 (1H, d, *J* 17.5 Hz), 5.33 (1H, d, *J* 10.7 Hz), 5.74 (1H, d, *J* 9.9 Hz), 6.63 (1H, dd, *J* 17.5, 10.7 Hz), 7.47 (1H, s).

Step 4. Mutilin 14-[*N*-(1-ethyl-piperidin-4-oyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-ethyl-piperidin-4-oyl)]-carbamate (110 mg) in 1,4-dioxane (0.7 ml) was treated with c.HCl (0.7 ml) and the solution was kept at room temperature for 2.5 hours. The solution was diluted with water (10 ml) and washed with dichloromethane (10 ml). The aqueous phase was basified by careful addition of solid potassium carbonate and the resulting mixture (pH 10) was extracted with chloroform (3 x 10 ml). The organic extract was dried (sodium sulphate) and the solvent was removed by evaporation under reduced pressure to give the title compound as a white solid (80 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 1.12 (3H, t, *J* 7.1 Hz), 2.48 (2H, q, *J* 7.1 Hz), 2.97 (3H, m), 3.37 (1H, dd, *J* 10.3, 6.6 Hz), 5.24 (1H, d, *J* 17.5 Hz), 5.37 (1H, d, *J* 11 Hz), 5.70 (1H, d, *J* 8.4 Hz), 6.50 (1H, dd, *J* 17.5, 11 Hz), 7.35 (1H, s); MS(EI) *m/z* 502 (M^+).

Example 88. Mutilin 14-{*N*-[1-(1-methyl-ethyl)-piperidin-4-oyl]}-carbamate

Step 1. Ethyl 1-(1-methyl-ethyl)-isonipecotate

Using the process described in Example 87, Step 1, ethyl isonipecotate (6.28 g) and 2-iodo-propane (7.48 g) were converted into the title compound, which was obtained as a pale yellow oil (7.17 g); MS(EI) *m/z* 199 (M^+).

Step 2. 1-(1-Methyl-ethyl)-isonipecotic acid hydrochloride

Using the process described in Example 87, Step 2, ethyl 1-(1-methyl-ethyl)-isonipecotate (6 g) was converted into the title compound, which was obtained as a white powder (6.1 g); MS(EI) *m/z* 171 (M^+).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[1-(1-methyl-ethyl)-piperidin-4-oyl]}-carbamate

Using the process described in Example 87, Step 3, 1-(1-methyl-ethyl)-isonipecotic acid hydrochloride (0.96 g) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1 g) were converted into the title compound, which was obtained as a pale yellow gum (195 mg); MS(EI) *m/z* 530 (M^+).

Step 4. Mutilin 14-{*N*-[1-(1-methyl-ethyl)-piperidin-4-oyl]}-carbamate

Using the process described in Example 87, Step 4, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[1-(1-methyl-ethyl)-piperidin-4-oyl]}-carbamate (170 mg) was converted into the title compound, which was obtained as a white solid (110 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 1.01 (6H, d, *J* 6.5 Hz), 2.74 (1H, m), 2.92 (3H, m), 3.37 (1H, dd, *J* 10.5, 6.6 Hz), 5.23 (1H, d, *J* 17.4 Hz), 5.36 (1H, d, *J* 11 Hz), 5.71 (1H, d, *J* 8.4 Hz), 6.50 (1H, dd, *J* 17.4, 11 Hz), 7.32 (1H, s); MS(EI) *m/z* 516 (M^+).

Example 89. Mutilin 14-{*N*-[1-(2-methoxy-ethyl)-piperidin-4-oyl]}-carbamate

Step 1. Ethyl 1-(2-methoxy-ethyl)-isonipecotate

Using the process described in Example 87, Step 1, ethyl isonipecotate (6.28 g) and 2-bromoethyl methyl ether (6.12 g) were converted into the title compound, which was obtained as a light yellow oil (8.47 g); MS(EI) *m/z* 216 (MH^+); Found: 216.1601, $C_{11}H_{22}NO_3$ requires 216.1599.

Step 2. 1-(2-Methoxy-ethyl)-isonipecotic acid hydrochloride

Using the process described in Example 87, Step 2, ethyl 1-(2-methoxy-ethyl)-isonipecotate (7.3 g) was converted into the title compound, which was obtained as a yellow gum (7.1 g); MS(EI) *m/z* 187 (M^+).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[1-(2-methoxy-ethyl)-piperidin-4-oyl]}-carbamate

Using the process described in Example 87, Step 3, 1-(2-methoxy-ethyl)-isonipecotic acid hydrochloride (0.98 g) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1 g) were converted into the title compound, which was obtained as a pale yellow solid (80 mg); MS(EI) *m/z* 546 (M^+).

Step 4. Mutilin 14-{*N*-[1-(2-methoxy-ethyl)-piperidin-4-oyl]}-carbamate

Using the process described in Example 87, Step 4, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[1-(2-methoxy-ethyl)-piperidin-4-oyl]}-carbamate (65 mg) was converted into the title compound, which was obtained as a white solid (50 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 2.58 (2H, t, 5.7 Hz), 3.00 (3H, m), 3.36 (4H, s overlapping m), 3.51 (2H, t, *J* 5.7 Hz), 5.24 (1H, d, *J* 17.3

Hz), 5.37 (1H, d, *J* 11Hz), 5.70 (1H, d, *J* 8.4 Hz), 6.50 (1H, dd, *J* 17.3, 11 Hz), 7.31 (1H, s); MS(EI) *m/z* 532 (M^+); Found: 532.3523. $C_{30}H_{48}N_2O_6$ requires 532.3512.

Example 90. Mutilin 14-[*N*-(1-propyl-piperidin-4-oyl)]-carbamate

Step 1. Ethyl 1-propyl-isonipecotate

Using the process described in Example 87, Step 1, ethyl isonipecotate (4.2 g) and propyl iodide (5 g) were converted into the title compound, which was obtained as a light yellow oil (4.39 g); MS(EI) *m/z* 199 (M^+).

Step 2. 1-propyl-isonipecotic acid hydrochloride

Using the process described in Example 87, Step 2, ethyl 1-propyl-isonipecotate (4.3 g) was converted into the title compound, which was obtained as an off-white solid (4.4 g); MS(EI) *m/z* 171 (M^+).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-propyl-piperidin-4-oyl)]-carbamate

Using the process described in Example 87, Step 3, 1-propyl-isonipecotic acid hydrochloride (0.5 g) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.5 g) were converted into the title compound, which was obtained as a colourless gum (65 mg); MS(EI) *m/z* 530 (M^+).

Step 4. Mutilin 14-[*N*-(1-propyl-piperidin-4-oyl)]-carbamate

Using the process described in Example 87, Step 4, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-propyl-piperidin-4-oyl)]-carbamate (50 mg) was converted into the title compound, which was obtained as a white solid (37 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 3.00 (3H, m), 3.36 (1H, dd, *J* 10. 6.6 Hz), 5.24 (1H, d, *J* 17.3 Hz), 5.36 (1H, d, *J* 11 Hz), 5.70 (1H, d, *J* 8.6 Hz), 6.48 (1H, dd, *J* 17.3, 11 Hz), 7.34 (1H, s); MS(EI) *m/z* 516 (M^+).

Example 91. Mutilin 14-[*N*-(quinuclidin-4-oyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(quinuclidin-4-oyl)]-carbamate

Using the process described in Example 87, Step 3, quinuclidine 4-carboxylic acid hydrochloride (*Helvetica Chimica Acta*, 1974, 57, 2332) (230 mg) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (330 mg) were converted into the title compound, which was obtained as a white foam (160 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 1.90 (6H, dd, *J* 8, 7.4 Hz), 3.10 (6H, dd, *J* 8, 7.4 Hz)), 3.21 (3H, s), 5.00 (1H, d, *J* 17.5 Hz), 5.27 (1H, d, *J* 10.7 Hz), 5.77 (1H, d, *J* 10 Hz), 6.68 (1H, dd, *J* 17.5, 10.7 Hz), 7.85 (1H, broad s); MS(ES) *m/z* 515 (MH^+).

Step 2. Mutilin 14-[*N*-(quinuclidin-4-oyl)]-carbamate

Using the process described in Example 87, Step 4, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(quinuclidin-4-oyl)]-carbamate (140 mg) was converted into the title compound, which was obtained as a white solid (86 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.7 Hz), 0.87 (3H, d, *J* 7 Hz), 1.17 (3H, s), 1.49 (3H, s), 1.68 (6H, dd, *J* 8, 7.3 z), 2.93 (6H, dd, *J* 8, 7.3 Hz), 3.34 (1H, dd, *J* 10, 6.6 Hz), 5.22 (1H, d, *J* 17.3 Hz), 5.36 (1H, d, *J* 11 Hz), 5.76 (1H, d, *J* 8.5 Hz), 6.54 (1H, dd, *J* 17.3, 11 Hz); MS(ES) *m/z* 501 (MH^+).

Example 92. Mutilin 14-[*N*-(quinuclidin-4-oyl)]-carbamate hydrochloride

Mutilin 14-[*N*-(quinuclidin-4-oyl)]-carbamate (71 mg) was dissolved in ethyl acetate (5 ml)/ 1,4-dioxane (2 ml) and 4*M* HCl in dioxane (0.2 ml) was added. The solution was concentrated to *ca.* 1 ml by evaporation of solvent under reduced pressure, and toluene (5 ml) was added to give a white precipitate. The precipitate was collected by filtration, washed with toluene (2 ml), and dried *in vacuo* to give the title compound as a white solid (79 mg); ^{1}H NMR (D_2O) *inter alia* 0.69 (3H, d, *J* 6 Hz), 0.92 (3H, d, *J* 6.8 Hz), 1.15 (3H, s), 1.39 (3H, s), 2.16 (6H, dd, *J* 8.2, 7.5 Hz), 3.42 (6H, dd, *J* 8.2, 7.5 Hz), 3.58 (1H, d, *J* 6 Hz), 5.20 (1H, d, *J* 17.5 Hz), 5.28 (1H, d, *J* 11.1 Hz), 5.68 (1H, d, *J* 8.1 Hz), 6.36 (1H, dd, *J* 17.5, 11.1 Hz).

Example 93. Mutilin 14-{*N*-(1-azabicyclo[2.2.1]heptan-4-oyl)}-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-(1-azabicyclo[2.2.1]heptan-4-oyl)}-carbamate

Using the process described in Example 87, Step 3, 1-azabicyclo[2.2.1]heptane 4-carboxylic acid hydrochloride (*Chemical Abstracts*, 1989, **110**, 95016) (700 mg) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1 g) were converted into the title compound, which was obtained as a white solid (330 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 2.05 (4H, m), 2.72 (4H, m), 3.08 (2H, m), 3.22 (3H, s), 3.44 (1H, m), 5.02 (1H, d, *J* 17.5 Hz), 5.30 (1H, d, *J* 11.6 Hz), 5.80 (1H, d, *J* 9.9 Hz), 6.69 (1H, dd, *J* 17.5, 11.6 Hz). 7.48 (1H, s); MS(ES) *m/z* 501 (MH^+).

Step 2. Mutilin 14-{*N*-(1-azabicyclo[2.2.1]heptan-4-oyl)}-carbamate

Using the process described in Example 87, Step 4, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-(1-azabicyclo[2.2.1]heptan-4-oyl)}-carbamate (300 mg) was converted into the title compound, which was obtained as a white solid (250 mg); ^{1}H NMR ($CDCl_3$) *inter alia* 2.28 (4H, m), 3.06 (2H, m), 3.37 (1H, broad s), 5.24 (1H, dd, *J* 17,3, 1.4 Hz), 5.38 (1H, dd, *J* 11, 1.4 Hz), 5.78 (1H, d, *J* 8.5 Hz), 6.64 (1H, dd, *J* 17.3, 11 Hz), 7.38 (1H, s); MS(EI) *m/z* 486 (M^+); Found: 486.3085, $C_{28}H_{42}N_2O_5$ requires 486.3094.

Example 94. Mutilin 14-[*N*-(*N*,*N*-dimethylcarbamoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(*N*,*N*-dimethylcarbamoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (270 mg, 0.80 mmol) was combined with dimethylcarbamoyl chloride (0.088 ml, 0.96 mmol) and silver cyanate (197 mg, 1.31 mmol) in dry dichloromethane (15 ml) and the reaction stirred at room temperature for 3 days in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 40% ethyl acetate in hexane. The title compound was isolated as a colourless foam (135 mg, 38%); ν_{max} (CH_2Cl_2) 3052, 2981, 1771, 1695, 1490 and 1459cm^{-1}; MS(CI) *m/z* 449 (MH^+), 466 (MNH_4^+).

Step 2. Mutilin-14-[*N*-(*N*,*N*-dimethylcarbamoyl)]-carbamate

The product of Step 1 (110 mg, 0.25 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml) and the reaction stirred at room temperature for 30 minutes. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 70% ethyl acetate in hexane to yield the title compound (90 mg, 83%); ν_{max} (CH_2Cl_2) 3402, 2935, 1774, 1735, 1686 and 1489cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.10-1.83 (16H, m) including 1.19 (3H, s) and 1.43 (3H, s), 2.06-2.37 (4H, m), 2.99 (6H, s), 3.37 (1H, dd, *J* 10.8, 6.7Hz), 5.20 (1H, dd, *J* 17.3, 1.5Hz), 5.36 (1H, dd, *J* 11.1, 1.5Hz), 5.71 (1H, d, *J* 8.4Hz), 6.53 (1H, dd, *J* 17.3, 11.1Hz), 6.54 (1H, bs); MS(CI) *m/z* 435 (MH^+).

Example 95. Mutilin 14-[*N*-(1-methyl (6H)-6-oxopyridine-3-carbonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-methyl (6H)-6-oxopyridine-3-carbonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500 mg, 1.50 mmol) was combined with 1-methyl (6H)-6-oxopyridine-3-carbonyl chloride (600 mg, 3.50 mmol) and silver cyanate (539 mg, 3.59 mmol) in dry dichloromethane (30 ml) and the reaction stirred at room temperature for 20 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 80% ethyl acetate in hexane. The title compound was isolated as a colourless foam (559 mg, 73%); ν_{max} (CH_2Cl_2) 3382, 2959, 1779, 1735, 1704 and 1473cm^{-1}; MS(CI) *m/z* 513 (MH^+), 530 (MNH_4^+).

Step 2. Mutilin-14-[*N*-(1-methyl (6H)-6-oxopyridine-3-carbonyl)]-carbamate

The product of Step 1 (550 mg, 1.07 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (5 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and

purified by chromatography on silica gel eluting with ethyl acetate to yield the title compound (360 mg, 67%); ν_{max} (CH_2Cl_2) 3427, 2935, 1778, 1734, 1662 and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.6Hz), 0.87 (3H, d, *J* 7.0Hz), 1.08-1.83 (16H, m) including 1.18 (3H, s) and 1.48 (3H, s), 2.08-2.34 (4H, m), 3.36 (1H, dd, *J* 10.8, 6.6Hz), 3.59 (3H, s), 5.22 (1H, dd, *J* 17.3, 1.5Hz), 5.38 (1H, dd, *J* 11.1, 1.5Hz), 5.79 (1H, d, *J* 8.5Hz), 6.52 (1H, dd, *J* 17.3, 11.1Hz), 6.54 (1H, d, *J* 9.5Hz), 7.62 (1H, dd, *J* 9.5, 2.6Hz), 7.87 (1H, bs), 8.16 (1H, d, *J* 2.6Hz); MS (EI) *m/z* 498 (M^+). Found: 498.2741, $C_{28}H_{38}N_2O_6$ requires 498.2730.

Example 96. Mutilin 14-[*N*-(6-chloronicotinoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(6-chloronicotinoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (250 mg, 0.75 mmol) was combined with 6-chloronicotinoyl chloride (1.21 g, 7.0 mmol) and silver cyanate (1.0 g, 6.67 mmol) in dry dichloromethane (15 ml) and the reaction stirred at room temperature for 10 minutes in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 20% ethyl acetate in hexane. The title compound was isolated as a colourless foam (311 mg, 80%); ν_{max} (CH_2Cl_2) 3413, 2930, 1780, 1719, 1697 and 1488cm^{-1}; MS(Cl) *m/z* 517 (MH^+), 534 (MNH_4^+).

Step 2. Mutilin-14-[*N*-(6-chloronicotinoyl)]-carbamate

The product of Step 1 (300 mg, 0.58 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane to yield the title compound (85 mg, 29%); ν_{max} (CH_2Cl_2) 3413, 2939, 1782, 1735, 1697, 1586 and 1489cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.07-1.82 (16H, m) including 1.18 (3H, s) and 1.50 (3H, s), 2.08-2.33 (4H, m), 3.36 (1H, dd, *J* 10.7, 6.6Hz), 5.21 (1H, dd, *J* 17.3, 1.5Hz), 5.33 (1H, dd, *J* 11.1, 1.5Hz), 5.79 (1H, d, *J* 8.5Hz), 6.49 (1H, dd, *J* 17.3,

11.1Hz), 7.45 (1H, d, *J* 8.3Hz), 8.07 (1H, dd, *J* 8.3, 2.3Hz), 8.08 (1H, bs), 8.74 (1H, d, *J* 2.3Hz); 6Hz); MS (EI) *m/z* 512 (M^+). Found: 512.2882, $C_{29}H_{40}N_2O_6$ requires 512.2886.

Example 97. Mutilin 14-[*N*-(2-methoxyisonicotinoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(2-methoxyisonicotinoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500 mg, 1.50 mmol) was combined with 2-methoxyisonicotinoyl chloride (600 mg, 3.2 mmol) and silver cyanate (500 mg, 3.30 mmol) in dry dichloromethane (20 ml) and the reaction stirred at room temperature for 3 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 30% ethyl acetate in hexane. The title compound was isolated as a colourless foam (598 mg, 78%); ν_{max} (CH_2Cl_2) 3410, 2931, 1781, 1720, 1698, 1559 and 1473cm^{-1}; MS(CI) *m/z* 517 (MH^+), 534 (MNH_4^+).

Step 2. Mutilin-14-[*N*-(2-methoxyisonicotinoyl)]-carbamate

The product of Step 1 (560 mg, 1.09 mmol) in dioxane (4 ml) was treated with a saturated solution of zinc chloride in conc. HCl (4 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane to yield the title compound (374 mg, 69%); ν_{max} (CH_2Cl_2) 3412, 2946, 1782, 1735, 1610, 1559 and 1474cm^{-1}; ^1H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.08-1.84 (16H, m) including 1.20 (3H, s) and 1.49 (3H, s), 2.10-2.37 (4H, m), 3.38 (1H, dd, *J* 10.6, 6.7Hz), 3.99 (3H, s), 5.24 (1H, dd, *J* 17.3, 1.5Hz), 5.39 (1H, dd, *J* 11.1, 1.5Hz), 5.72 (1H, d, *J* 8.5Hz), 6.53 (1H, dd, *J* 17.3, 11.1Hz), 7.05 (1H, d, *J* 1.1Hz), 7.18 (1H, dd, *J* 5.2, 1.1Hz), 7.92 (1H, bs), 8.31 (1H, d, *J* 5.2Hz); MS (EI) *m/z* 498 (M^+). Found: 498.2726, $C_{28}H_{29}N_2O_6$ requires 498.2730.

Example 98. Mutilin 14-[*N*-(morpholine-4-ylcarbonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(morpholine-4-ylcarbonyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 g, 3.0 mmol) was combined with 4-morpholine carbonyl chloride (1.40 ml, 12.0 mmol) and silver cyanate (2.0 g, 13.3 mmol) in dry dichloromethane (45 ml) and the reaction stirred at room temperature for 17 days in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 50% ethyl acetate in hexane. The title compound was isolated as a colourless foam (990 mg, 67%); ν_{max} (CH_2Cl_2) 3394, 2985, 1771, 1736, 1695 and 1421cm^{-1}; MS(CI) *m/z* 491 (MH^+).

Step 2. Mutilin-14-[*N*-(morpholine-4-ylcarbonyl)]-carbamate

The product of Step 1 (500 mg, 1.02 mmol) in dioxane (5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (5 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 70% ethyl acetate in hexane to yield the title compound (180 mg, 37%); ν_{max} (CH_2Cl_2) 3391, 2928, 1773, 1735, 1684, 1488 and 1458cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.6Hz), 0.85 (3H, d, *J* 7.0Hz), 1.06-1.82 (16H, m) including 1.18 (3H, s) and 1.42 (3H, s), 2.04-2.38 (4H, m), 3.33 (1H, dd, *J* 10.4, 6.6Hz), 3.45 (4H, m), 3.70 (4H, m), 5.20 (1H, dd, *J* 17.3, 1.5Hz), 5.32 (1H, dd, *J* 11.1, 1.5Hz), 5.69 (1H, d, *J* 8.4Hz), 6.51 (1H, dd, *J* 17.3, 11.1Hz), 6.68 (1H, bs); MS (CI) *m/z* 477 (MH^+).

Example 99. Mutilin 14-[*N*-(thiomorpholine-4-ylcarbonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(thiomorpholine-4-ylcarbonyl)]-carbamate

A solution of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (250 mg, 0.75 mmol) in diethyl ether (5 ml) was added to a solution of *N*-(chlorocarbonyl)-

isocyanate (0.060 ml, 0.75 mmol) in diethyl ether (5 ml) under an atmosphere of argon at -50°C. The temperature was raised to 0°C over 1.5 hours and then a solution of thiomorpholine (0.075 ml, 0.75 mmol) and triethylamine (0.079 ml, 0.75 mmol) in diethyl ether (5 ml) was added dropwise. The reaction mixture was stirred for 2 hours at room temperature and then partitioned between 0.5M hydrochloric acid and ethyl acetate. The organic layer was washed with brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 30% ethyl acetate in hexane. The title compound was isolated as a colourless foam (144 mg, 38%); ν_{max} (CH_2Cl_2) 3393, 2928, 1771, 1739, 1682 and 1458cm^{-1}; MS(Electrospray) *m/z* 505 $[M-H]^-$.

Step 2. Mutilin-14-[*N*-(thiomorpholine-4-ylcarbonyl)]-carbamate

The product of Step 1 (170 mg, 0.34 mmol) in dioxane (1.5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.5 ml) and the reaction stirred at room temperature for 1 hour. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane to yield the title compound (115 mg, 69%); ν_{max} (CH_2Cl_2) 3393, 2930, 1772, 1736, 1682, 1458 and 1426cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.75 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.09-1.83 (16H, m) including 1.18 (3H, s) and 1.45 (3H, s), 2.04-2.35 (4H, m), 2.69 (4H, m), 3.34 (1H, dd, *J* 10.6, 6.6Hz), 3.73 (4H, m), 5.20 (1H, dd, *J* 17.3, 1.5Hz), 5.33 (1H, dd, *J* 11.1, 1.5Hz), 5.69 (1H, d, *J* 8.7Hz), 6.50 (1H, dd, *J* 17.3, 11.1Hz), 6.65 (1H, bs); MS (CI) *m/z* 493 (MH^+).

Example 100. Mutilin 14-[*N*-(thiomorpholine-4-ylcarbonyl-1,1-dioxide)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(thiomorpholine-4-ylcarbonyl-1,1-dioxide)]-carbamate

A solution of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(thiomorpholine-4-ylcarbonyl)]carbamate (120 mg, 0.24 mmol) in methanol (2 ml) was cooled to 0°C and treated with a solution of oxone (442 mg, 0.72 mmol) in water (2 ml). The reaction mixture was stirred for 1 hour at room temperature and then partitioned between water and dichloromethane. The organic layer was washed with water and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 50% ethyl acetate in

hexane. The title compound was isolated as a colourless foam (73 mg, 57%); ν_{max} (CH_2Cl_2) 3387, 2931, 1775, 1742, 1694 and 1461cm^{-1}; MS(CI) *m/z* 539 (MH^+).

Step 2. Mutilin-14-[*N*-(thiomorpholine-4-ylcarbonyl-1,1-dioxide)]-carbamate

The product of Step 1 (220 mg, 0.40 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 80% ethyl acetate in hexane to yield the title compound (120 mg, 57%); ν_{max} (CH_2Cl_2) 3388, 2938, 1776, 1736, 1692, 1465 and 1426cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.72 (3H, d, *J* 6.6Hz), 0.90 (3H, d, *J* 7.0Hz), 1.09-1.83 (16H, m) including 1.18 (3H, s) and 1.42 (3H, s), 2.07-2.34 (4H, m), 3.18 (4H, m), 3.37 (1H, dd, *J* 10.6, 6.5Hz), 3.92 (4H, m), 5.22 (1H, dd, *J* 17.3, 1.5Hz), 5.33 (1H, dd, *J* 11.1, 1.5Hz), 5.67 (1H, d, *J* 8.4Hz), 6.46 (1H, dd, *J* 17.3, 11.1Hz), 6.80 (1H, bs); MS (CI) *m/z* 542 (MNH_4^+).

Example 101. Mutilin 14-[*N*-(1-methylpiperazin-4-ylcarbonyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-methylpiperazin-4-ylcarbonyl)]-carbamate

A solution of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500 mg, 1.5 mmol) in diethyl ether (10 ml) was added to a solution of *N*-(chlorocarbonyl)-isocyanate (0.12 ml, 1.5 mmol) in diethyl ether (10 ml) under an atmosphere of argon at -50°C. The temperature was raised to 0°C over 1.5 hours and then a solution of 1-methylpiperazine (0.16 ml, 1.5 mmol) and triethylamine (0.16 ml, 1.5 mmol) in diethyl ether (10 ml) was added dropwise. The reaction mixture was stirred for 2 hours at room temperature and then partitioned between 0.5M hydrochloric acid and ethyl acetate. The organic layer was washed with brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 20% methanol in ethyl acetate. The title compound was isolated as a colourless foam (170 mg, 23%); ν_{max} (CH_2Cl_2) 3394, 2942, 1769, 1740, 1684 and 1458cm^{-1}; MS(CI) *m/z* 504 (MH^+).

Step 2. Mutilin-14-[*N*-(1-methylpiperazin-4-ylcarbonyl)]-carbamate

The product of Step 1 (165 mg, 0.32 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room temperature for 3 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 30% methanol in ethyl acetate to yield the title compound (81 mg, 52%); ν_{max} (CH_2Cl_2) 3392, 2941, 1771, 1736, 1683, 1488 and 1458cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.75 (3H, d, *J* 6.6Hz), 0.86 (3H, d, *J* 7.0Hz), 1.00-1.80 (16H, m) including 1.12 (3H, s) and 1.38 (3H, s), 2.02-2.25 (4H, m), 2.30 (3H, s), 2.41 (4H, m), 3.35 (1H, m), 3.45 (4H, m), 5.20 (1H, dd, *J* 17.3, 1.5Hz), 5.35 (1H, dd, *J* 11.1, 1.5Hz), 5.70 (1H, d, *J* 8.4Hz), 6.50 (1H, dd, *J* 17.3, 11.1Hz), 6.60 (1H, bs); MS (CI) *m/z* 490 (MH^+).

Example 102. Mutilin 14-[*N*-(4-{4-(2-morpholinoethyloxy)}-benzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-acetoxybenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 mg, 3.0 mmol) was combined with 4-acetoxybenzoyl chloride (2.3 g, 11.0 mmol) and silver cyanate (1.7 g, 11.3 mmol) in dry dichloromethane (30 ml) and the reaction stirred at room temperature for 3 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 40% ethyl acetate in hexane. The title compound was isolated as a colourless foam (1.5 g, 93%); ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, *J* 6.6Hz), 1.02 (3H, d, *J* 7.0Hz), 1.10-1.77 (12H, m) including 1.22 (3H, s) and 1.30 (3H, s), 1.69-1.76 (2H, m), 1.95-2.05 (2H, m), 2.22 (1H, m), 2.32 (3H, s), 2.53 (1H, dd, *J* 15.3, 10.1Hz), 2.90 (1H, q, *J* 6.5Hz), 3.20 (3H, s), 3.47 (1H, m), 5.02 (1H, d, *J* 17.5Hz), 5.30 (1H, d, *J* 10.7Hz), 5.87 (1H, d, *J* 10.0Hz), 6.72 (1H, dd, *J* 17.5, 10.7Hz), 7.20 (2H, d, *J* 8.7Hz), 7.88 (2H,d, *J* 8.7Hz), 7.95 (1H, bs).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxybenzoyl)]-carbamate

The product of Step 1 (1.50 g, 2.78 mmol) in dioxane (20 ml) was treated with 1M aqueous sodium hydroxide solution (9 ml). The reaction mixture was stirred at room temperature for 30 minutes under an atmosphere of argon. The mixture was diluted with ethyl acetate and dilute aqueous hydrochloric acid, the layers separated, and the organic phase washed with brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 50% ethyl acetate in hexane. The title compound was isolated as a colourless foam (1.30 g, 94%); ^1H NMR ($CDCl_3$) 0.89 (3H, d, *J* 6.6Hz), 1.00 (3H, d, *J* 7.0Hz), 1.09-1.70 (12H, m) including 1.20 (3H, s) and 1.30 (3H, s), 1.70-1.79 (2H, m), 1.97-2.03 (2H, m), 2.20 (1H, m), 2.53 (1H, dd, *J* 15.3, 10.1Hz), 2.92 (1H, q, *J* 6.5Hz), 3.23 (3H, s), 3.49 (1H, m), 5.01 (1H, d, *J* 17.5Hz), 5.29 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 10.0Hz), 6.12 (1H,exch), 6.70 (1H, dd, *J* 17.5, 10.7Hz), 6.94 (2H, d, *J* 8.7Hz), 7.74 (2H,d, *J* 8.7Hz), 7.94 (1H, bs).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-{4-(2-morpholinoethyloxy)}benzoyl)]-carbamate

The product of Step 2 (700 mg, 1.41 mmol) in acetone (14 ml) was treated with potassium carbonate (389 mg, 2.82 mmol) and 4-(2-chloroethyl)morpholine hydrochloride (262mg, 1.41 mmol). The reaction mixture was heated to reflux for 16 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and water and the layers separated. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 5% ethanol in ethyl acetate. The title compound was isolated as a colourless foam (275 mg, 32%); ν_{max} (CH_2Cl_2) 3421, 2932, 1774, 1726, 1698, 1605 and 1474cm^{-1}; MS(Electrospray) *m/z* 611 (MH^+).

Step 4. Mutilin-14-[*N*-(4-{4-(2-morpholinoethyloxy)}benzoyl)]-carbamate

The product of Step 3 (265 mg, 0.43 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room temperature for 1 hour. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 70% ethyl acetate in hexane to yield the title compound (160 mg, 62%); ν_{max} (CH_2Cl_2) 3418, 2939, 1775, 1732, 1605 and 1476cm^{-1}; ^1H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.6Hz), 0.86 (3H, d,

J 7.0Hz), 1.10-1.82 (16H, m) including 1.15 (3H, s) and 1.49 (3H, s), 2.08-2.39 (4H, m), 2.54 (4H, m), 2.80 (2H, t, *J* 5.7Hz), 3.36 (1H, dd, *J* 10.8, 6.5Hz), 3.72 (4H, m), 4.13 (2H, t, *J* 5.7Hz), 5.21 (1H, dd, *J* 17.3, 1.5Hz), 5.37 (1H, dd, *J* 11.1, 1.5Hz), 5.82 (1H, d, *J* 8.4Hz), 6.55 (1H, dd, *J* 17.3, 11.1Hz), 6.92 (2H, d, *J* 8.9Hz), 7.78 (2H, d, *J* 8.9Hz), 7.83 (1H, bs); MS(CI) *m/z* 597 (MH^+).

Example 103. Mutilin 14-[*N*-(3-(2-dimethylaminoethoxy)-benzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-acetoxybenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 mg, 3.0 mmol) was combined with 3-acetoxybenzoyl chloride (1.8 g, 8.4 mmol) and silver cyanate (1.31 g, 8.7 mmol) in dry dichloromethane (30 ml) and the reaction stirred at room temperature for 2 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 5% ethyl acetate in dichloromethane to yield the title compound (960 mg, 59%); ν_{max} (CH_2Cl_2) 3414, 2929, 1775, 1715, 1698 and 1475cm^{-1}; MS (EI) *m/z* 539 (M^+). Found: 539.2883, $C_{31}H_{41}NO$, requires 539.2883.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-hydroxybenzoyl)]-carbamate

The product of Step 1 (940 mg, 1.74 mmol) in dioxane (14 ml) was treated with 1M aqueous sodium hydroxide solution (5.6 ml). The reaction mixture was stirred at room temperature for 30 minutes under an atmosphere of argon. The mixture was diluted with ethyl acetate and dilute aqueous hydrochloric acid, the layers separated, and the organic phase washed with brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 40% ethyl acetate in hexane to yield the title compound (629 mg, 73%); ν_{max} (CH_2Cl_2) 3575, 3414, 2929, 1776, 1713, 1697 and 1479cm^{-1}; MS (CI) *m/z* 498 (MH^+), 515 (MNH_4^+).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-(2-dimethylaminoethoxy)benzoyl)]-carbamate

The product of Step 2 (590 mg, 1.19 mmol) in acetone (10 ml) was treated with potassium carbonate (328 mg, 2.38 mmol) and 2-dimethylaminoethyl chloride

hydrochloride (171mg, 1.19 mmol). The reaction mixture was heated to reflux for 16 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and water and the layers separated. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 10% ethanol in ethyl acetate to yield the title compound (138 mg, 20%); ν_{max} (CH_2Cl_2) 3419, 2943, 1776, 1713, 1698, 1583 and 1477cm^{-1}; MS (EI) *m/z* 568 (M^+). Found: 568.3516, $C_{33}H_{48}N_2O_6$ requires 568.3512.

Step 4. Mutilin-14-[*N*-(3-(2-dimethylaminoethoxy)benzoyl)]-carbamate

The product of Step 3 (120 mg, 0.21 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 3% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (69 mg, 59%); ν_{max} (CH_2Cl_2) 3412, 2961, 1778, 1732, 1706 and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.15-1.83 (16H, m) including 1.19 (3H, s) and 1.52 (3H, s), 2.03-2.28 (4H, m), 2.34 (6H, s), 2.74 (2H, t, *J* 5.6Hz), 3.39 (1H, m), 4.10 (2H, t, *J* 5.6Hz), 5.22 (1H, dd, *J* 17.3, 1.5Hz), 5.39 (1H, dd, *J* 11.1, 1.5Hz), 5.83 (1H, d, *J* 8.4Hz), 6.56 (1H, dd, *J* 17.3, 11.1Hz), 7.12 (1H, m), 7.28-7.40 (3H, m), 7.92 (1H, bs); MS (EI) *m/z* 554 (M^+). Found: 554.3368, $C_{32}H_{48}N_2O_6$ requires 554.3356.

Example 104. Mutilin 14-[*N*-(4-(3-dimethylaminopropyl)-benzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-(3-dimethylaminopropyl)benzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxy-benzoyl)]-carbamate (370 mg, 0.74 mmol) in acetone (10 ml) was treated with potassium carbonate (207 mg, 1.50 mmol) and 3-dimethylaminopropyl chloride hydrochloride (118 mg, 0.75 mmol). The reaction mixture was heated to reflux for 16 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and water, and the layers separated. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 5% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (170

mg, 39%); ν_{max} (CH_2Cl_2) 3425, 2943, 1774, 1697, 1605 and 1468cm^{-1}; MS (EI) *m/z* 582 (M^+). Found: 582.3675, $C_{34}H_{50}N_2O_6$ requires 582.3669.

Step 2. Mutilin-14-[*N*-(4-(3-dimethylaminopropyl)benzoyl)]-carbamate

The product of Step 1 (152 mg, 0.26 mmol) in dioxane (1 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml) and the reaction stirred at room temperature for 1.5 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 5% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (80 mg, 54%); ν_{max} (CH_2Cl_2) 3418, 2956, 1775, 1732, 1605 and 1477cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.78 (3H, d, *J* 6.6Hz), 0.87 (3H, d, *J* 7.0Hz), 1.05-1.85 (16H, m) including 1.18 (3H, s) and 1.50 (3H, s), 1.95-2.30 (6H, m), 2.34 (6H, s), 2.55 (2H, t, *J* 7.1Hz), 3.42 (1H, m), 4.08 (2H, t, *J* 6.3Hz), 5.21 (1H, dd, *J* 17.3, 1.5Hz), 5.37 (1H, dd, *J* 11.1, 1.5Hz), 5.82 (1H, d, *J* 8.4Hz), 6.56 (1H, dd, *J* 17.3, 11.1Hz), 6.93 (2H, d, *J* 8.8Hz), 7.74 (2H, d, *J* 8.8Hz), 7.85 (1H, bs); MS (EI) *m/z* 568 (M^+). Found: 568.3499, $C_{33}H_{48}N_2O_6$ requires 568.3512.

Example 105. Mutilin 14-[*N*-(4-[2-pyrrolidin-1-yl-ethoxy])-benzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-[2-pyrrolidin-1-yl-ethoxy]benzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxy-benzoyl)]-carbamate (600 mg, 1.21 mmol) in acetone (10 ml) was treated with potassium carbonate (333 mg, 2.41 mmol) and 1-(2-chloroethyl)pyrrolidine hydrochloride (205 mg, 1.21 mmol). The reaction mixture was heated to reflux for 16 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and water and the layers separated. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 3% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (302 mg, 42%); ν_{max} (CH_2Cl_2) 3053, 2985, 1774, 1697, 1605 and 1421cm^{-1}; MS (CI) *m/z* 595 (MH^+).

Step 2. Mutilin-14-[*N*-(4-[2-pyrrolidin-1-yl-ethoxy]benzoyl)]-carbamate

The product of Step 1 (280 mg, 0.47 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 4% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (52 mg, 19%); ν_{max} (CH_2Cl_2) 3427, 1775, 1732, 1711, 1606 and 1478cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.79 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.10-1.85 (20H, m) including 1.18 (3H, s) and 1.52 (3H, s), 2.09-2.40 (4H, m), 2.62 (4H, m), 2.92 (2H, t, *J* 5.8Hz), 3.46 (1H, m), 4.12 (2H, t, *J* 5.8Hz), 5.22 (1H, dd, *J* 17.3, 1.5Hz), 5.38 (1H, dd, *J* 11.1, 1.5Hz), 5.82 (1H, d, *J* 8.4Hz), 6.58 (1H, dd, *J* 17.3, 11.1Hz), 6.97 (2H, d, *J* 8.8Hz), 7.75 (2H, d, *J* 8.8Hz), 7.80 (1H, bs); MS (CI) *m/z* 581 (MH^+).

Example 106. Mutilin 14-[*N*-(4-[3-(4-methylpiperazin-1-yl)-propyloxy]-benzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-[3-(4-methylpiperazin-1-yl)-propyloxy]benzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxybenzoyl)]-carbamate (600 mg, 1.21 mmol) in acetone (10 ml) was treated with potassium carbonate (480 mg, 3.47 mmol) and 1-(3-chloropropyl)-4-methylpiperazine dihydrochloride (302 mg, 1.21 mmol). The reaction mixture was heated to reflux for 16 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and water and the layers separated. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 5% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (230 mg, 30%); ν_{max} (CH_2Cl_2) 3420, 2941, 1774, 1697, 1605 and 1467cm^{-1}; MS (EI) *m/z* 637 (M^+). Found: 637.4085, $C_{37}H_{55}N_3O_6$ requires 637.4091.

Step 2. Mutilin-14-[*N*-(4-[3-(4-methylpiperazin-1-yl)-propyloxy]benzoyl)]-carbamate

The product of Step 1 (200 mg, 0.31 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and

saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 5% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (80 mg, 41%); ν_{max} (KBr) 3427, 2924, 1753, 1727, 1689, 1605 and 1465cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.87 (3H, d, *J* 7.0Hz), 1.14-2.52 (35H, m) including 1.18 (3H, s), 1.52 (3H, s) and 2.29 (3H, s), 3.36 (1H, m), 4.08 (2H, t, *J* 6.3Hz), 5.21 (1H, dd, *J* 17.3, 1.5Hz), 5.38 (1H, dd, *J* 11.1, 1.5Hz), 5.82 (1H, d, *J* 8.4Hz), 6.57 (1H, dd, *J* 17.3, 11.1Hz), 6.94 (2H, d, *J* 8.8Hz), 7.73 (2H, d, *J* 8.8Hz), 7.81 (1H, bs); MS (EI) *m/z* 623 (M^+). Found: 623.3921, $C_{36}H_{53}N_3O_6$ requires 623.3921.

Example 107. Mutilin 14-[*N*-(3-fluoro-4-hydroxybenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-acetoxy-3-fluorobenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 mg, 3.0 mmol) was combined with 4-acetoxy-3-fluorobenzoyl chloride (1.7 g, 7.5 mmol) and silver cyanate (1.20 g, 8.0 mmol) in dry dichloromethane (30 ml) and the reaction stirred at room temperature for 2 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 5% ethyl acetate in dichloromethane to yield the title compound (1.61 g, 96%); ν_{max} (CH_2Cl_2) 3413, 2930, 1777, 1716, 1697 and 1479cm^{-1}; MS (CI) *m/z* 575 (MNH_4^+).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-fluoro-4-hydroxybenzoyl)]-carbamate

The product of Step 1 (1.59 g, 2.85 mmol) in dioxane (20 ml) was treated with 1M aqueous sodium hydroxide solution (9 ml). The reaction mixture was stirred at room temperature for 30 minutes under an atmosphere of argon. The mixture was diluted with ethyl acetate and dilute aqueous hydrochloric acid, the layers separated, and the organic phase washed with brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 40% ethyl acetate in hexane to yield the title compound (1.42 g, 96%); ν_{max}

(CH_2Cl_2) 3547, 3417, 2930, 1776, 1713, 1697, 1618 and 1479cm^{-1}; MS (Electrospray) *m/z* 514 $[M-H]^-$.

Step 3. Mutilin-14-[*N*-(3-fluoro-4-hydroxybenzoyl)]-carbamate

The product of Step 2 (200 mg, 0.39 mmol) in dioxane (1 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at room temperature for 1.5 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 60% ethyl acetate in hexane to yield the title compound (110 mg, 56%); ν_{max} (KBr) 3307, 2931, 1731, 1690, 1618, 1504 and 1457cm^{-1}; ^1H NMR ($CDCl_3$ + d_6DMSO) 0.72 (3H, d, *J* 6.6Hz), 0.83 (3H, d, *J* 7.0Hz), 1.05-1.76 (16H, m) including 1.10 (3H, s) and 1.42 (3H, s), 1.85-2.34 (5H, m), 3.39 (1H, dd, *J* 10.1, 6.6Hz), 5.13 (1H, dd, *J* 17.3, 1.5Hz), 5.26 (1H, dd, *J* 11.1, 1.5Hz), 5.72 (1H, d, *J* 8.4Hz), 6.50 (1H, dd, *J* 17.3, 11.1Hz), 6.92 (1H, m), 7.45 (1H, m), 7.58 (1H,m), 8.99 (1H, bs); MS (CI) *m/z* 519 (MNH_4^+).

Example 108. Mutilin 14-[*N*-(4-[2-dimethylaminoethoxy]-3-fluorobenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-[2-dimethylaminoethoxy]-3-fluorobenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-fluoro-4-hydroxybenzoyl)]-carbamate (613 mg, 1.19 mmol) in acetone (10 ml) was treated with potassium carbonate (328 mg, 2.38 mmol) and 2-dimethylaminoethyl chloride hydrochloride (171 mg, 1.19 mmol). The reaction mixture was heated to reflux for 16 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and water and the layers separated. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 2% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (360 mg, 52%); ν_{max} (CH_2Cl_2) 3419, 2943, 1776, 1697, 1615 and 1497cm^{-1}; MS (CI) *m/z* 587 (MH^+).

Step 2. Mutilin-14-[*N*-(4-[dimethylaminoethoxy]-3-fluorobenzoyl)]-carbamate

The product of Step 1 (350 mg, 0.59 mmol) in dioxane (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml) and the reaction stirred at

room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 5% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (203 mg, 60%); ν_{max} (CH_2Cl_2) 3414, 2944, 1777, 1732, 1713, 1615 and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.16-1.83 (16H, m) including 1.18 (3H, s) and 1.49 (3H, s), 2.10-2.29 (4H, m), 2.33 (6H, s), 2.79 (2H, t, *J* 5.7Hz), 3.36 (1H, m), 4.17 (2H, t, *J* 5.7Hz), 5.21 (1H, dd, *J* 17.3, 1.5Hz), 5.38 (1H, dd, *J* 11.1, 1.5Hz), 5.82 (1H, d, *J* 8.4Hz), 6.54 (1H, dd, *J* 17.3, 11.1Hz), 7.01 (1H, m), 7.52-7.60 (2H, m), 7.82 (1H, bs); MS (CI) *m/z* 573 (MH^+).

Example 109. Mutilin 14-[*N*-(4-[2-dimethylaminoethoxy]-3-methoxybenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-acetoxy-3-methoxybenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.0 mg, 3.0 mmol) was combined with 4-acetoxy-3-methoxybenzoyl chloride (820 mg, 4.75 mmol) and silver cyanate (715 mg, 4.77 mmol) in dry dichloromethane (30 ml) and the reaction stirred at room temperature for 2 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 50% ethyl acetate in dichloromethane to yield the title compound (1.37 g, 80%); ν_{max} (CH_2Cl_2) 3417, 2931, 1775, 1713, 1698, 1604 and 1479cm^{-1}; MS (EI) *m/z* 569 (M^+). Found: 569.2991, $C_{32}H_{43}NO_8$ requires 569.2989.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxy-3-methoxybenzoyl)]-carbamate

The product of Step 1 (1.30 mg, 2.28 mmol) in dioxane (20 ml) was treated with 1M aqueous sodium hydroxide solution (7.3 ml). The reaction mixture was stirred at room temperature for 2 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and dilute aqueous hydrochloric acid, the layers separated, and the organic phase washed with brine. After drying

($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 20% ethyl acetate in dichloromethane to yield the title compound (1.08 g, 90%); ν_{max} (CH_2Cl_2) 3519, 3424, 2930, 1773, 1697 and 1479cm^{-1}; MS (EI) *m/z* 527 (M^+). Found: 527.2889, $C_{30}H_{41}NO_7$ requires 527.2883.

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-4-[2-dimethylaminoethoxy]-3-methoxybenzoyl)]-carbamate

The product of Step 2 (1.04 g, 1.97 mmol) in acetone (20 ml) was treated with potassium carbonate (545 mg, 3.95 mmol) and 2-dimethylaminoethyl chloride hydrochloride (284 mg, 1.97 mmol). The reaction mixture was heated to reflux for 16 hours under an atmosphere of argon. The mixture was diluted with ethyl acetate and water and the layers separated. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 4% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (185 mg, 16%); ν_{max} (CH_2Cl_2) 3421, 2941, 1773, 1697, 1599 and 1477cm^{-1}; MS (CI) *m/z* 599 (MH^+).

Step 4. Mutilin-14-[*N*-4-[2-dimethylaminoethoxy]-3-methoxybenzoyl)]-carbamate

The product of Step 3 (160 mg, 0.27 mmol) in dioxane (1.5 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1.5 ml) and the reaction stirred at room temperature for 2 hours. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate and the combined organic phases were washed with saturated sodium chloride solution. The organic phase was dried ($MgSO_4$) and purified by chromatography on silica gel eluting with 4% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (65 mg, 41%); ν_{max} (CH_2Cl_2) 3418, 2962, 1776, 1732, 1600 and 1478cm^{-1}; ^1H NMR ($CDCl_3$) 0.80 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 7.0Hz), 1.12-1.90 (16H, m) including 1.19 (3H, s) and 1.52 (3H, s), 2.05-2.30 (4H, m), 2.35 (6H, s), 2.80 (2H, t, *J* 6.0Hz), 3.39 (1H, m), 3.90 (3H, s), 4.12 (2H, t, *J* 6.0Hz), 5.23 (1H, dd, *J* 17.3, 1.5Hz), 5.39 (1H, dd, *J* 11.1, 1.5Hz), 5.85 (1H, d, *J* 8.4Hz), 6.58 (1H, dd, *J* 17.3, 11.1Hz), 6.90 (1H, m), 7.29-7.42 (2H, m), 7.85 (1H, bs); MS (EI) *m/z* 584 (M^+). Found: 584.3474, $C_{33}H_{48}N_2O_7$ requires 584.3474.

Example 110. Mutilin 14-{*N*-[(3*S*,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl]}-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[(3*S*,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl]}-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (490 mg, 1.46 mmol) was combined with (3*S*,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl chloride (280 mg, 1.46 mmol) and silver cyanate (550 mg, 3.67 mmol) in dry dichloromethane (20 ml). Triethylamine (0.20 ml, 1.46 mmol) was added and the reaction stirred at room temperature for 16 hours in subdued light and under an atmosphere of argon. The mixture was filtered through Kieselguhr and the filtrate washed with saturated aqueous sodium hydrogen carbonate (x2) and brine. After drying ($MgSO_4$) purification was accomplished by chromatography on silica gel eluting with 4% (9:1 methanol:ammonia (35%)) in dichloromethane to yield the title compound (276 mg, 38%); ν_{max} (CH_2Cl_2) 3383, 2981, 1780, 1749, 1698, 1460 and 1374cm^{-1}; MS (EI) *m/z* 500 (M^+). Found: 500.3248, $C_{29}H_{44}N_2O_5$ requires 500.3250.

Step 2. Mutilin-14 {*N*-[(3S,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl]}-carbamate

The product of Step 1 (260 mg, 0.52 mmol) in dioxane (3 ml) was treated with conc. HCl (3 ml) and the reaction stirred at room for 30 minutes. The solution was diluted with water and washed with dichloromethane (x2). The aqueous phase was basified with saturated aqueous sodium hydrogen carbonate and the product extracted into dichloromethane.. The organic phase was dried ($MgSO_4$) and concentrated to yield the title compound (187 mg, 74%); ν_{max} (CH_2Cl_2) 3386, 2962, 1782, 1735, 1699 and 1467cm^{-1}; ^{1}H NMR (d_6-DMSO) 0.63 (3H, d, *J* 6.6Hz), 0.81 (3H, d, *J* 7.0Hz), 1.05-3.12 (29H, m) including 1.09 (3H, s) and 1.42 (3H, s), 4.52 (1H, d, *J* 6.0Hz, exch), 5.03-5.12 (2H, m), 5.51 (1H, d, *J* 7.8Hz), 6.21 (1H, dd, *J* 17.7, 11.1Hz), 10 40 (1H, bs); MS(CI) *m/z* 487 (MH^+).

Example 111. Mutilin 14-(piperidin-4-oyl)-carbamate

Step 1. Mutilin 11-dichloroacetyl-14-(1-*tert*-butoxycarbonylpiperidin-4-oyl)-carbamate

1-*tert*-Butoxycarbonylpiperidine-4-carboxylic acid [*J. Med. Chem.*, (1996), 39(10), 1943-5] (229mg) was converted to the acid chloride with oxalyl chloride (152mg, 0.105ml) and 1 drop of DMF in dichloromethane. Silver cyanate

(300mg) was added to the reaction mixture and the mixture refluxed for 1hr. After cooling mutilin 11-dichloroacetate (216mg) and tetrakis(triphenylphosphine)-palladium(0) (5mg) was added and the reaction mixture stirred at room temperature for 16h. The mixture was filtered through celite and the solvent removed from the filtrate *in vacuo*. Following purification by silica gel chromatography the title compound was obtained as a colourless foam, (154mg, 45%); ν_{max} (CH_2Cl_2) 3382, 1786, 1754, 1736, 1686 and 1473 cm^{-1}; MS(CI) m/z 702 $(M+NH_4)^+$.

Step 2. Mutilin 14-(1-*tert*-butoxycarbonylpiperidin-4-oyl)-carbamate

Mutilin 11-dichloroacetate-14-(1-*tert*-butoxycarbonylpiperidin-4-oyl)-carbamate (150mg) in tetrahydrofuran (1ml) was treated with 1M aqueous sodium hydroxide (1.5ml) and vigorously stirred at room temperature for 1.5hr. The reaction mixture was diluted with ethyl acetate and washed with 5% citric acid, brine, dried over anhydrous magnesium sulfate and concentrated. After purification by silica gel chromatography, the title compound was obtained as a colourless solid, (47mg, 37%); ν_{max} (CH_2Cl_2) 3385, 1784, 1735, 1699 and 1686 cm^{-1}; MS(CI) m/z 575 $(M+H)^+$.

Step 3. Mutilin 14-(piperidin-4-oyl)-carbamate

Mutilin 14-(1-*tert*-butoxycarbonylpiperidin-4-oyl)-carbamate (45mg) in dichloromethane at room temperature was treated with trifluoroacetic acid (90mg, 0.06ml) and the solution left 16h. The solution was concentrated and dried *in vacuo* to a colourless solid, (36mg, 97%); Crystallization from acetone/hexane afforded the title compound as colourless prisms, m.p. 190-195 °C; ν_{max} (CH_2Cl_2) 3382, 1780, 1735, 1704 and 1677 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.6Hz), 0.90 (3H, d, *J* 6.8Hz), 1.19 (3H, s), 1.43 (3H, s), 2.87 (2H, t, *J* 11.6Hz), 3.32 (3H, m), 5.23 (1H, d, *J* 18.6Hz), 5.35 (1H, d, *J* 11.1Hz), 5.69 (1H, d, *J* 8.4Hz), 6.48 (1H, dd, *J* 11.1,18.6Hz) and 7.90 (1H, vbr s); MS(CI) m/z 475 $(M+H)^+$.

Example 112. Mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-6-oyl)-carbamate

Step1. 2,3-Dihydroimidazol[1,2-b]thiazole-6-carboxylic acid

Ethyl 2,3-dihydroimidazol[1,2-b]thiazole-6-carboxylate, (Patent, WO 94/10178, 11th May 1994) (760mg) in ethanol (5ml) was hydrolysed with aqueous sodium hydroxide at 60 °C for 3hr. The solvent was removed *in vacuo* and the residue re-

dissolved in water and acidified to pH 3 with 5M hydrochloric acid. No precipitate was formed. The aqueous solution was freeze-dried and the solid residue extracted with hot ethanol. After filtration and removal of solvent the title compound was obtained as a pale yellow amorphous solid, (621mg, quant.); ^{1}HNMR ($CDCl_3$) 3.93 (2H, t, *J* 7.0Hz), 4.25 (2H, t, *J* 7.6Hz) and 7.93 (1H, s).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-6-oyl)-carbamate

A suspension of 2,3-dihydroimidazol[1,2-b]thiazole-6-carboxylic acid (316mg) in dry dichloromethane (3ml) was treated with oxalyl chloride (381mg, 0.26ml) for 3hr. The slurry that was formed was concentrated *in vacuo* to remove excess oxalyl chloride and the solid residue re-suspended in dry dichloromethane. The reaction mixture was cooled in an ice bath and triethylamine (202mg, 0.28ml) was slowly added. The pale yellow solution/solid was warmed to room temperature and silver cyanate (600mg) was added. The mixture was stirred at room temperature 16h. and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (334mg) added. The reaction mixture was stirred for 2h. The mixture was filtered through celite. The filtrate was then washed with water, saturated aqueous sodium hydrogen carbonate dried over anhydrous magnesium sulfate and concentrated. Purification by silica gel chromatography eluting with 80% and then 90% ethyl acetate/hexane afforded the title compound as a colourless foam, (113mg, 21%); ν_{max} (CH_2Cl_2) 3374, 1769,1728,1698, 1543, 1945 and 1468 cm^{-1}; MS(CI) m/z 530 $(M+H)^+$.

Step 3. Mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-6-oyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-6-oyl)-carbamate (214mg) in dioxan (1ml) was treated at room temperature with Lukas reagent (1ml). The reaction was exothermic and darkened. After 1h, t.l.c. analysis showed complete conversion to the product. The reaction mixture was diluted with ethyl acetate and neutralized with saturated aqueous sodium hydrogen carbonate. The aqueous phase was extracted with ethyl acetate and the combined organic phases washed with brine, dried over anhydrous magnesium sulfate and concentrated to a colourless solid. Trituration with dichloromethane and filtering gave the title compound as a white amorphous solid, (97mg, 47%); ν_{max} (KBr) 1762, 1732, 1637, 1543, 1509 and 1464 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.63 (3H, d, *J* 6.0Hz), 0.81 (3H, d, *J* 6.7Hz), 1.05 (3H, s), 1.39 (3H, s), 3.41 (1H, d, *J* 5.5Hz), 3.90 (2H, t, *J* 7.0Hz) 4.24 (2H, t, *J* 7.0Hz), 5.09 (2H, m), 5.53 (7.8Hz), 6.20 (1H, dd, *J* 11.2,17.6Hz), 7.98 (1H, s) and 9.66 (1H, s exchangeable with D_2O); MS(ES) m/z 516 $(M+H)^+$.

Example 113. Mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-5-oyl)-carbamate

Step1. 2,3-Dihydroimidazol[1,2-b]thiazole-5-carboxylic acid

Ethyl 2,3-dihydroimidazol[1,2-b]thiazole-5-carboxylate (formed as a side-product in the preparation of the thiazol-6-carboxylate, Example 112) (3.84g) was hydrolysed to the acid with aqueous sodium hydroxide (50ml) as described in Example 112, Step 1. After acidification a white precipitate was formed. This was filtered off, washed with water and dried overnight *in vacuo*. The title compound was obtained as a white solid, (2.86g, 93%); ^{1}HNMR (d6-DMSO) 3.96 (2H, t, *J* 7.3Hz), 4.37 (2H, t, *J* 7.3Hz), 7.51 (1H, s) and 12.89 (1H vbr s).

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-5-oyl)-carbamate

2,3-dihydroimidazol[1,2-b]thiazole-5-carboxylic acid (316mg) was converted to the acid chloride and coupled to (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin on the same scale, and using the same procedure described in Example 112, Step 2. Purification by silica gel chromatography using 50% and then 60% ethyl acetate/hexane afforded the title compound as a colourless solid, (353, 67%); ν_{max} (CH_2Cl_2) 3419, 1769, 1723, 1697, 1520 and 1484 cm^{-1}; MS(EI) m/z 529 (M^+).

Step 3. Mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-5-oyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2,3-dihydroimidazol[2,1-b]thiazol-5-oyl)-carbamate (324mg) in dioxan (2ml) was treated with concentrated hydrochloric acid (1ml) at room temperature for 2days. The reaction mixture was worked up as described in Example 113, Step 3. The resultant colourless foam crystallized on addition of dichloromethane. The title compound was obtained as a colourless crystalline solid, (206mg, 65%); ν_{max} (KBr) 1735, 1712, 1527 and 1433 cm^{-1}; ^{1}HNMR (d_6-DMSO) *inter alia* 0.67 (3H, d, *J* 5.9Hz), 0.83 (3H, d, *J* 6.8Hz), 1.08 (3H, s) 1.45 (3H, s), 3.45 (1H, t, *J* 5.5Hz), 3.95 (2H, d, *J* 7.8Hz), 4.54 (1H, d, *J* 6.0Hz), 5.09 (2H, m), 5.60 (1H, d, *J* 7.9Hz), 7.87 (1H, s) and 10.5 (1H, s); MS(CI) m/z 515 (M^+); Found: 515.2458, $C_{27}H_{37}N_3O_5S$ requires 515.2452.

Example 114. Mutilin 14-(1-Methylpiperidin-4-oyl)-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(1-methylpiperidin-4-oyl)-carbamate

1-Methylpiperidin-4-carboxylic acid (500mg) was converted to the corresponding acid chloride with thionyl chloride [*J. Med. Chem.*, (1990), 33(6), 1599]. A suspension of the acid chloride in dry dichloromethane (5ml) was treated with silver cyanate (1.04g) and the reaction mixture refluxed for 1h. After cooling, (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (334mg) was added followed by triethylamine (281mg, 0.39ml) after 10m. The reaction mixture was filtered through celite, and the filtrate washed with saturated aqueous sodium hydrogen carbonate. Following purification by silica gel chromatography, the title compound was obtained as a colourless foam, (426mg, 85%); ν_{max} (CH_2Cl_2) 3381, 1781, 1749, 1698 and 1474 cm^{-1}; MS(EI) m/z 502 (M^+); Found: 502.3411, $C_{29}H_{46}N_2O_5$ requires 502.3407.

Step 2. Mutilin 14-(1-methylpiperidin-4-oyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(1-methylpiperidin-4-oyl)-carbamate (1.08g) in dioxan (8ml), was treated wih concentrated hydrochloric acid (4ml) at room temperature for 5h. T.l.c. analysis showed complete conversion to the product. The solvents were removed *in vacuo* and the residual material dissolved in water. The solution was extracted with dichloromethane. The aqueous solution was basified with saturated aqueous sodium hydrogen carbonate to pH 8 and extracted with dichloromethane (three times). The combined organic phases were subsequently washed with brine, dried over anhydrous magnesium sulfate and concentrated to give a colourless foam. Trituration with hexane afforded the title compound as a colourless amporphous solid, (574mg, 55%); ν_{max} (CH_2Cl_2) 3385, 1782, 1736, 1704 and 1474 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 7.0Hz), 1.18 (3H, s), 1.42 (3H, s), 2.28 (3H, s), 3.36 (1H, dd, *J* 6.7,10.2Hz), 5.22 (1H, d, *J* 17.5Hz), 5.36 (1H, d, *J* 11.0Hz), 5.70 (1H, d, *J* 8.4Hz), 6.49 (1H, dd, *J* 11.0,17.3Hz) and 7.43 (1H, s);MS(EI) m/z 488 (M^+), Found: 488.3225, $C_{28}H_{44}N_2O_5$ requires 488.3250.

Example 115. Mutilin 14-(1-Methylpiperidin-4-oyl)-carbamate Hydrochloride salt

Mutilin 14-(1-methylpiperidin-4-oyl)-carbamate (350mg) in ethyl acetate (5ml) at room temperature was treated with a solution of 4M hydrogen chloride in dioxan

in a dropwise fashion until no more precipitate was formed. The white solid was removed by filtration, washed with ethyl acetate and dried *in vacuo*. The title compound was obtained as an amporphous white solid, (300mgs, 80%); ^{1}HNMR (D_2O) *inter alia* 0.69 (3H, d, *J* 5.8Hz), 0.92 (3H, d, *J* 6.8Hz), 1.14 (3H, s), 1.38 (3H, s), 2.89 (3H, s), 3.05 (2H, t, *J* 12.7Hz), 5.19 (1H, d, *J* 17.5Hz), 5.26 (1H, d, *J* 11.1Hz), 5.61 (1H, d, *J* 8.1Hz) and 6.35 (1H, d, *J* 11.1,17.5Hz).

Example 116. Mutilin 14-(2-Chloropropionyl)-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2Chloropropionyl)-carbamate

3-Chloropropionyl chloride (889mg, 0.67ml), silver cyanate (2.05g) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (668mg), in dichloromethane (10ml) were allowed to react at room temperature for 3 days. The mixture was filtered through celite, washed with saturated aqueous sodium hydrogen carbonate, dried over anhydrous magnesium sulfate and concentrated, to give a gum. Purification by silica gel chromatography afforded the title compound as a crisp white foam, (909mg, 97%); ν_{max} (CH_2Cl_2) 3382, 1785, 1752, 1711, 1699 and 1473 cm^{-1}; MS(CI) m/z 485 $(M+NH_4)^+$.

Step 2. Mutilin 14-(2-Chloropropionyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2-chloro-propionyl)-carbamate (300mg) in dioxan (2ml), cooled to 0-5 °C was treated with Lukas reagent (2ml) and allowed to warm to room temperature. After 2h, the reaction mixture was diluted with dichloromethane and washed with water, saturated aqueous sodium hydrogen carbonate, brine and then dried over anhydrous magnesium sulfate. After purification by silica gel chromatography, the title compound was obtained as a colourless foam, (223mg, 77%); ν_{max} (CH_2Cl_2) 3624, 3564, 3384, 1786, 1754, 1734, 1710 and 1473 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.74 (3H, d, *J* 6.8Hz), 0.89 (3H, d, *J* 7.0Hz), 1.19 (3H, s), 1.42 (3H, s), 3.29 (2H, t, *J* 7.0Hz), 3.37 (1H, dd, *J* 6.7,10.7Hz), 3.80 (3H, t, *J* 7.0Hz), 5.24 (1H, d, *J* 17.4Hz), 5.34 (1H, d, *J* 11.0Hz), 5.70 (1H, d, *J* 8.5Hz), 6.48 (1H, dd, *J* 11.0,17.4Hz) and 7.50 (1H, s); MS(ES) m/z 452 $(M-H)^-$.

Example 117. Mutilin 14-(2-diethylaminopropionyl)-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2-Diethylaminopropionyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2-chloropropionyl)-carbamate (200mg) in ethyl acetate (2ml) at room temperature was treated with diethylamine (312mg, 0.44ml). After 2h, no remaining starting material by t.l.c. analysis. The solution was washed with saturated aqueous sodium hydrogen carbonate, water (two times), brine and then dried over anhydrous magnesium sulfate. The solution was concentrated to give the title compound as a colourless foam, (197mg, 92%); ν_{max} (CH_2Cl_2) 1770, 1697, 1520 and 1458 cm^{-1}; MS(EI) m/z 504 (M^+), Found: 504.3548, $C_{29}H_{48}N_2O_5$ requires 504.3563.

Step 2. Mutilin 14-(2-diethylaminopropionyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(2-diethylaminopropionyl)-carbamate, (320mg) was converted to the title compound as described in Example 116, Step 2. The product was obtained as a colourless foam, (153mg, 49%); ν_{max} (CH_2Cl_2) 1772, 1735, 1703 and 1520 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.76 (3H, d, *J* 6.6Hz), 0.87 (3H, d, *J* 7.0Hz), 1.08 (6H, t, *J* 7.2Hz), 1.17 (3H, s), 1.43 (3H, s), 3.34 (1H, dd, *J* 6.5,11.2Hz), 5.21 (1H, d, *J* 17.4Hz), 5.37 (1H, d, *J* 11.0Hz), 5.71 (1H, d, *J* 8.5Hz) and 6.59 (1H, dd, *J* 11.0,17.4Hz); MS(EI) m/z 490 (M^+), Found: 490.3414, $C_{28}H_{46}N_2O_5$ requires 490.3407.

Example 118. Mutilin 14-(Acryloyl)-carbamate

Step 1. Mutilin 14-(acryoyl)-carbamate

Mutilin 14-(2-chloropropionyl)-carbamate (150mg) in dichloromethane (1ml) at room temperature was treated with triethylamine (67mg, 0.092ml). After 2h., t.l.c. analysis showed no starting material, The solution was purified by silica gel chromatography to give the title compound as a colourless foam, (135mg, 98%); ν_{max} (CH_2Cl_2) 3625, 3563, 3389, 1779, 1735, 1697, 1625 and 1485 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.75 (3H, d, *J* 6.8Hz), 0.89 (3H, d, *J* 7.0Hz), 1.12 (3H, s), 1.45 (3H, s), 3.37 (1H, dd, *J* 6.6,10.7Hz), 5.23 (1H, d, *J* 17.3Hz), 5.37 (1H, d, *J* 11.1Hz), 5.72 (1H, d, *J* 8.5Hz), 5.89 (1H, d, *J* 10.4Hz), 6.50 (2H, dd, *J* 10.4,17.4Hz), 7.06 (1H, dd, *J* 11.1,17.3Hz) and 7.60 (1H, s); MS(CI) m/z 435 $(M+NH_4)^+$.

Example 119. Mutilin 14-(1-Benzylpiperidin-4-oyl)-carbamate

Step 1. 1-Benzylpiperidine-4-carboxylic acid

Ethyl 1-benzylpiperidine-4-carboxylate (13.73g) in methanol (100ml) was treated with 40% aqueous sodium hydroxide (8.3ml) at room temperature 16h. The solvent was removed *in vacuo* and the residue re-dissolved in water (100ml), acidified with dilute hydrochloric acid to pH 4 and concentrated. The residue was extracted with hot ethanol (200ml), filtered and concentrated again. Addition of dichloromethane resulted in crystallization giving the title compound as a colourless crystaline solid, (3.24g, 27%). Removal of solvent from the filtrate and trituration with ether gave a second batch as an amorphous white solid, (9.24g, 73%); ν_{max} (CH_2Cl_2) 2496 (vbr), 1720 and 1604 (br) cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(1-Benzylpiperidin-4-oyl)-carbamate

1-Benzylpiperidine-4-carboxylic acid (500mg) in dichloromethane (5ml) was converted to the acid chloride with oxalyl chloride (319mg, 0.22ml) and 1 drop of DMF over 1h. To this homogeneous solution was added silver cyanate (684mg) and the reaction mixture refluxed for 1h. The mixture was cooled to room temperature and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (334mg) added. After 5m, triethylamine (0.32ml) was added dropwise. After 2h. the reaction mixture was filtered through celite, washed with water, saturated aqueous sodium hydrogen carbonate, brine and dried over anhydrous magnesium sulfate. Removal of solvent *in vacuo*, and purification of the residue by silica gel chromatography, afforded the title compound as a colourless foam, (355mg, 61%); ν_{max} (CH_2Cl_2) 3384, 1782, 1784, 1699 and 1478 cm^{-1}; MS(ES) m/z 579 $(M+H)^+$.

Step 3. Mutilin 14-(1-Benzylpiperidin-4-oyl)-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(1-benzylpiperidin-4-oyl)-carbamate (304mg) in dioxan (0.5ml) was treated with concentrated hydrochloric acid (0.5ml) until t.l.c. analysis showed no starting material. The solvents were removed under vacuum and the residue partitioned between saturated aqueous sodium hydrogen carbonate and dichloromethane. The organic phase was dried over anhydrous magnesium sulfate and the solvent removed *in vacuo*. The crude product was purified by silica gel chromatography to give the title compound as a foam, (172mg, 58%); ν_{max} (CH_2Cl_2) 3622, 3562, 3383, 1782, 1735, 1703 and 1477 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.72 (3H, d, *J*

6.6Hz), 0.88 (3H, d, *J* 7.0Hz), 1.18 (3H, s), 1.42 (3H, s), 3.36 (1H, dd, *J* 6.6,10.5Hz), 3.51 (2H, s), 5.21 (1H, d, *J* 17.3Hz), 5.35 (1H, d, *J* 10.9Hz), 5.69 (1H, d, *J* 8.4Hz), 6.48 (1H, d, *J* 10.9,17.3Hz) and 7.30 (4H, m); MS(CI) m/z 564 (M^+), Found: 564.3538, $C_{34}H_{48}N_2O_5$ requires 564.3564.

Example 120. Mutilin 14-[1-(4-Methoxybenzyl)piperidin-4-oyl]-carbamate

Step 1. Ethyl 1-(4-methoxybenzyl)piperidine-4-carboxylate

Ethyl isonipecotate (5g, 4.9ml) and 4-methoxybenzyl chloride (5g, 4.44ml) in DMF (40ml) with potassium carbonate (8.8g) was heated to 70 °C for 2h, then room temperature for 2days, and again at 70 °C for 2h. The reaction mixture was partitioned between ethyl acetate/water. The organic layer was washed with water (2x), brine, dried over anhydrous magnesium sulfate and concentrated.The title compound was obtained as a yellow oil, (8.05g, quant.); ν_{max} (CH_2Cl_2) 1725, 1611, 1585, 1511 and 1466 cm^{-1}; MS(EI) m/z 277 (M^+), Found: 277.1682, $C_{16}H_{23}NO_3$ requires 277.1678.

Step 2. 1-(4-methoxybenzyl)piperidine-4-carboxylic acid

Ethyl 1-(4-methoxybenzyl)piperidine-4-carboxylate, (8.05g) was hydrolysed to the corresponding acid with sodium hydroxide as described in Example 119, Step 1. Following isolation of the crude product, the foam was triturated with ether overnight to give the title compound as a white, crystalline solid, (6.23g, 86%); ν_{max} (KBr) 1731, 1613, 1516 and1457 cm^{-1}; MS(EI) m/z 249 (M^+), Found 249.1368, $C_{14}H_{19}NO_3$ requires 249.1365.

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[1-(4-methoxybenzyl)piperidin-4-oyl]-carbamate

1-(4-Methoxybenzyl)piperidine-4-carboxylic acid (747mg) was converted to the acid chloride with oxalyl chloride (0.27ml) in dichloromethane (10ml) and then reacted with silver cyanate (600mg) and coupled to (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500mg) in the presence of triethylamine (0.42ml) as described in example 119, Step 2. After purification the title compound was obtained as a colourless foam, (515mg, 56%); ν_{max} (CH_2Cl_2) 3383, 1782, 1749, 1699, 1611, 1511 and 1468 cm^{-1}; MS(EI) m/z 608 (M^+), Found: 608.3813, $C_{36}H_{52}N_2O_6$ requires 608.3825.

Step 4. Mutilin 14-[1-(4-Methoxybenzyl)piperidin-4-oyl]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[1-(4-methoxybenzyl)piperidin-4-oyl]-carbamate (485mg) in dioxan (2ml) was converted to the title compound as described in Example 119, Step 3. After purification the product was obtained as a colourless foam, (433mg, 92%); ν_{max} (CH_2Cl_2) 3624, 3565, 3385, 1783, 1734, 1705, 1611, 1511 and 1468 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.7Hz), 0.89 (3H, d, *J* 6.9Hz), 1.18 (3H, s), 1.43 (3H, s), 2.61 (2H, s), 3.81 (3H, s), 5.22 (1H, d, *J* 19.4Hz), 5.36 (1H, d, *J* 11.1Hz), 5.70 (1H, d, *J* 8.0Hz), 6.49 (1H, dd, *J* 11.1,19.4Hz), 6.85 (2H, d, *J* 8.6Hz), 7.22 (2H, d, *J* 8.6Hz) and 7.32 (1H, s); MS(EI) m/z 594 (M^+), Found: 594.3657, $C_{35}H_{50}N_2O_6$ requires 594.3669.

Example 121. Mutilin 14-[1-(4-Methoxybenzyl)piperidin-4-oyl]-carbamate Hydrochloride salt

Mutilin 14-[1-(4-methoxybenzyl)piperidin-4-oyl]-carbamate (100mg) in ethyl acetate (1ml) was treated with 4M hydrogen chloride in dioxan, dropwise until no further precipitation was observed. The white solid was filtered off, washed with ethyl acetate and dried under vacuum. The title compound was obtained as an amorphous white solid, (70mg, 66%); ^{1}HNMR (d_6-DMSO) *inter alia* 0.63 (3H, d, *J* 6.2Hz), 0.83 (3H, d, *J* 6.7Hz), 1.08 (3H, s), 1.40 (3H, s), 3.79 (3H, s), 4.20 (2H, br s), 4.56 (1H, d, *J* 5.9Hz), 5.06 (1H, d, *J* 11.0Hz), 5.10 (1H, d, *J* 17.6Hz), 5.50 (1H, d, *J* 7.8Hz), 6.22 (1H, dd, *J* 11.0,17.6Hz), 7.01 (2H, d, *J* 8.5Hz), 7.50 (2H, d, *J* 8.5Hz), 10.30 (1H, br s) and 10.51 (1H, s).

Example 122. Mutilin 14-[1-(4-Fluorobenzyl)piperidin-4-oyl]-carbamate

Step 1. Ethyl 1-(4-Fluorobenzyl)piperidine-4-carboxylate

Ethyl isonipecotate (5g, 4.9ml) was alkylated with 4-fluorobenzyl bromide, (6.02g, 3.97ml) in DMF (40ml) in the presence of potassium carbonate (8.8g) as described in Example 120, Step 1. The title compound was obtained as a yellow oil, (7.52g, 89%); ν_{max} (CH_2Cl_2) 1725, 1603, 1508 and 1449 cm^{-1}; MS(EI) m/z 265 (M^+), Found: 265.1478, $C_{15}H_{20}FNO_2$ requires 265.1478.

Step 2. 1-(4-Fluorobenzyl)piperidine-4-carboxylic acid

Ethyl 1-(4-fluorobenzyl)piperidine-4-carboxylate (7.52g) was hydrolysed with 40% sodium hydroxide (4.3ml) as described in Example 120, Step 2. After work-up the title compound was obtained as a colourless solid, (4.26g, 63%); ν_{max} (KBr) 1722, 1605, 1511 and 1447 cm^{-1}; MS(EI) m/z 237 (M^+), Found: 237.1160, $C_{13}H_{16}FNO_2$ requires 237.1165.

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[1-(4-Fluorobenzyl)piperidin-4-oyl]-carbamate

1-(4-Fluorobenzyl)piperidine-4-carboxylic acid (711mg) was converted to the acid chloride with oxalyl chloride (0.27ml), treated with silver cyanate (600mg) and coupled to (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500mg) in the presence of triethylamine (0.42ml) as described in Example 120, Step 3. Following purification the title compound was isolated as a colourless foam, (539mg, 60%); ν_{max} (CH_2Cl_2) 3678, 3381, 1781, 1748, 1699, 1603, 1508 and 1478 cm^{-1}; MS(ES) m/z 597 $(MH)^+$.

Step 4. Mutilin 14-[1-(4-Fluorobenzyl)piperidin-4-oyl]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[1-(4-fluorobenzyl)piperidin-4-oyl]-carbamate (510mg) was converted to the title compound as described in Example 120, Step 4. After purification the product was obtained as a colourless foam, (346mg, 70%); ν_{max} (CH_2Cl_2) 3563, 3386, 1783, 1735, 1705, 1604, 1508 and 1478 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.72 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 8.0Hz), 1.19 (3H, s), 1.43 (3H, s), 3.37 (1H, dd, *J* 6.6,10.2Hz), 3.45 (2H, s), 5.22 (1H, d, *J* 17.5Hz), 5.36 (1H, d, *J* 9.9Hz), 5.70 (1H, d, *J* 8.4Hz), 6.49 (1H, dd, *J* 9.9,17.5Hz), 7.00 (2H, m), 7.26 (2H, m) and 7.35 (1H, s); MS(EI) m/z 582 (M^+), Found: 582.3472, $C_{35}H_{47}FN_2O_5$ requires 582.3469.

Example 123. Mutilin 14-[1-(pyridin-2-ylmethyl)piperidin-4-oyl]-carbamate

Step 1. Ethyl 1-(pyridin-2-ylmethyl)piperidine-4-carboxylate

Ethyl isonipecotate (4.79g, 4.7ml) was alkylated with 2-chloromethylpyridine hydrochloride (5g) and potassium carbonate (12.62g) in DMF (40ml) as described in Example 120, Step 1. The title compound was obtained as a yellow

oil, (6,09g, 81%); ν_{max} (CH_2Cl_2) 1724, 1590, 1570, 1476, 1449 and 1433 cm^{-1}; MS(ES) m/z 249 $(MH)^+$.

Step 2. 1-(pyridin-2-ylmethyl)piperidine-4-carboxylic acid

Ethyl 1-(pyridin-2-ylmethyl)piperidine-4-carboxylate (6.08g) was hydrolysed with 40% sodium hydroxide (3.7ml) in methanol (50ml) as dscribed in Example 120, Step 2. After isolation the title compound was obtained as a pale green foam, (5.01g, 93%). A portion of the material was shown to crystallize from dichloromethane to give a colourless crystalline solid; ν_{max} (KBr) 1685 (br), 1601 and 1463 cm^{-1}; MS(ES) m/z 221 $(MH)^+$.

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[1-(pyridin-2-ylmethyl)piperidin-4-oyl]-carbamate

1-(Pyridin-2-ylmethyl)piperidine-4-carboxylic acid (440mg) was coverted to the acid chloride with oxalyl chloride (267mg, 0.18ml) and treated with silver cyanate (450mg) and then coupled to (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (334mg) in the presence of triethylamine (0.28ml), as described in Example 120, Step 3. After purification the title compound was isolated as a pale yellow foam, (267mg, 46%); ν_{max} (CH_2Cl_2) 3382, 1782, 1749, 1699, 1590 and 1475 cm^{-1}; MS(EI) m/z 580 $(MH)^+$, Found: 580.3741, $C_{34}H_{50}N_3O_5$ requires 580.3750.

Step 4. Mutilin 14-[1-(pyridin-2-ylmethyl)piperidin-4-oyl]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[1-(pyridin-2-ylmethyl)piperidin-4-oyl]-carbamate (248mg) was converted with concentrated hydrochloric acid as described in Example 120, Step 4. After work-up, the crude product was re-dissolved in dilute hydrochloric acid washed with dichloromethane, basified with saturated aqueous sodium hydrogen carbonate and re-extracted. After drying and removal of solvent the title compound was obtained as a pale yellow solid, (135mg, 56%); ν_{max} (CH_2Cl_2) 3676, 3622, 3564, 3384, 1782, 1735, 1703, 1590 and 1475 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 6.9Hz), 1.18 (3H, s), 1.42 (3H, s), 3.36 (1H, dd, *J* 6.6,10.5Hz), 3.67 (3H, s), 5.22 (1H, d, *J* 17.3Hz), 5.36 (1H, d, *J* 11.1Hz), 5.70 (1H, d, *J* 8.4Hz), 6.49 (1H, dd, *J* 11.1,17.3Hz), 7.17 (1H, m), 7.45 (2H, m), 7.66 (1H, m) and 8.55 (1H, d, *J* 4.0Hz); MS (ES) *m/z* 565 (M^+); Found 565.3527, $C_{33}H_{47}N_3O_5$ requires 565.3516.

Example 124. Mutilin 14-{1-[(2-methylthiazol-4-yl)methyl]-piperidin-4-oyl}-carbamate

Step 1. Ethyl 1-[(2-methylthiazol-4-yl)methyl]piperidine-4-carboxylate

Ethyl isonipecotate (3.14g, 3.08ml) was alkylated with 4-chloromethyl-2-methylthiazole hydrochloride (3.68g) in DMF (40ml) with potassium carbonate (8.28g) as peviously described in Example 120, Step 1. After purification by silica gel chromatography the title compound was isolated as a yellow oil, (3.26g, 61%); ν_{max} (CH_2Cl_2) 1724 cm^{-1}; MS(EI) m/z 269 $(MH)^+$, Found: 269.1318, $C_{13}H_{21}N_2O_2S$ requires 269.1324.

Step 2. 1-[(2-methylthiazol-4-yl)methyl]piperidine-4-carboxylic acid

Ethyl 1-[(2-methylthiazol-4-yl)methyl]piperidine-4-carboxylate (3.06g) was hydrolysed to the acid with 40% sodium hydroxide (1.73ml) as described in Example 120, Step 2. After purification the title compound was isolated as a colourless solid, (3.08g, 99%); ν_{max} (KBr) 1719, 1665, 1591 and 1392 cm^{-1}; MS(EI) m/z 240 (M^+), Found: 240.0934, $C_{11}H_{16}N_2O_2S$ requires 240.0932.

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{1-[(2-methylthiazol-4-yl)methyl]piperidin-4-oyl}-carbamate

1-[(2-Methylthiazol-4-yl)methyl]piperidine-4-carboxylic acid (720mg) was converted to the acid chloride with oxalyl chloride (0.27ml), treated with silver cyanate (600mg) and coupled to (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (500mg) in the presence of triethylamine (0.42ml), as previously outlined in Example 120, Step 3. Following purification the title compound was obtained as a pale yellow foam, (405mg, 45%); ν_{max} (CH_2Cl_2) 3382, 1781, 1784, 1698 and 1478 cm^{-1}; MS (EI) *m/z* 599 (M^+); Found 599.3406, $C_{33}H_{49}N_3O_5S$ requires 599.3392.

Step 4. Mutilin 14-{1-[(2-methylthiazol-4-yl)methyl]piperidin-4-oyl}-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{1-[(2-methylthiazol-4-yl)methyl]piperidin-4-oyl}-carbamate (391mg) was converted to the title compound as described in Example 121, Step 4. The product was obtained as a white solid, (241mg, 63%); ν_{max} (CH_2Cl_2) 3677, 3384, 1783, 1735, 1705 and 1477 cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.6Hz), 0.89 (3H, d, *J* 6.9Hz), 1.18 (3H, s), 1.42 (3H, s), 2.71 (3H, s), 2.99 (2H, d, *J* 10.3Hz), 3.36 (1H, dd, *J* 6.6,10.5Hz), 3.63 (2H, s), 5.24 (1H, d, *J* 17.0Hz), 5.36

(1H, d, *J* 11.1Hz), 5.72 (1H, d, *J* 8.4Hz), 6.48 (1H, dd, *J* 11.1,17.0Hz), 6.95 (1H, s) and 7.38 (1H, s).

Example 125. Mutilin 14-(*N*-3-pyridylacetyl)-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-3-pyridylacetyl)-carbamate

3-Pyridylacetic acid (520 mg, 3 mmol) in dichloromethane (5 ml) was treated with oxalyl chloride (0.45 ml, 5.2 mmol) and one drop of DMF at room temperature for 2h. The solvent and excess oxalyl chloride were removed *in vacuo*. The residue was dissolved in toluene and the solvent again removed *in vacuo*.

The crude acid chloride in dry dichloromethane (10 ml) was treated with silver cyanate (900 mg, 6 mmol) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1 mmol). After stirring at room temperature for 18h the title compound was isolated by the procedure described in Example 31, Step 2, (360 mg, 72%); ν_{max} (CH_2Cl_2) 3380, 1752 and 1699 cm^{-1}; ^1H NMR ($CDCl_3$) 0.80 (3H, d, J6.9Hz), 1.01 (3H, d, J6.4Hz), 1.08-1.37 (3H, m), 1.19 (3H, s), 1.21 (3H, s), 1.56 (4H, m), 1.73 (1H, d, J11.3Hz), 1.99 (2H, m), 2.20 (1H, m), 2.49 (1H, dd, J15.2, 10.1Hz), 2.88 (1H, q, J6.3Hz), 3.21 (3H, s), 3.44 (1H, m), 4.18 (2H, m), 5.04 (1H, d, J17.5Hz), 5.34 (1H, d, J10.8Hz), 5.74 (1H, d, J9.9Hz), 6.62 (1H, dd, J17.5, 10.6Hz), 7.28 (2H, m), 7.65 (1H, dt, J 7.8, 1.9Hz) 7.72 (1H, s), 8.54 (1H, s); MS (NH_3 DCI) *m/z* 497 (MH^+), Found: 496.2948, $C_{29}H_{40}N_2O_5$ requires 496.2937.

Step 2. Mutilin 14-(*N*-3-pyridylacetyl)-carbamate

The product from step 1, (310 mg) in dioxan (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml), as for Example 1 Step 2, to afford the title compound, (173 mg, 58%); ν_{max} (CH_2Cl_2) 3383, 1754, 1734, 1716 cm^{-1}; ^1H NMR ($CDCl_3$) 0.70 (3H, d, J6.7Hz), 0.91 (3H, d, J7.0Hz), 1.17 (1H, m), 1.19 (3H, s), 1.40 (3H, s), 1.36-1.82 (8H, m), 2.05-2.36 (5H, m), 3.37 (1H, dd, J10.1, 6.7Hz), 4.14 (2H, AB quartet, J 16.3Hz), 5.24 (1H, dd, J17.4, 1.4Hz), 5.39 (1H, dd, J11.1, 1.3Hz), 5.71 (1H, d, J8.4Hz), 6.49 (1H, dd, J17.4, 11.0Hz), 7.26 (1H, m), 7.56 (1H, s), 7.63 (1H, d, J7.8Hz), 8.52 (2H, m); MS (NH_3 DCI) *m/z* 483 (MH^+), Found: 483.2856, $C_{28}H_{38}N_2O_5$ requires 483.2859.

Example 126. Mutilin 14-(*N*-2-pyridylmethyl)-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-(*N*-2-pyridylmethyl)-carbamate

2-Aminomethylpyridine (0.31 ml, 3 mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin-14-chloroformate (400 mg, 1 mmol) in dichloromethane (10 ml), as for Example 12 Step 2, to afford the title compound (463mg, 98%); ν_{max} (CH_2Cl_2) 3446, 1709 cm^{-1}; ^1H NMR ($CDCl_3$) 0.85 (3H, d, J6.9Hz), 0.98 (3H, d, J6.5Hz), 1.05-1.61 (6H, m), 1.19 (3H, s), 1.22 (3H, s), 1.68 (1H, d, J15.3Hz), 1.71 (1H, d, J11.2Hz), 1.99 (2H, m), 2.19 (1H, m), 2.43 (1H, dd, J15.1, 10.1Hz), 2.94 (1H, q, J6.4Hz), 3.22 (3H, s), 3.46 (1H, ddd, J11.3, 8.2, 5.3Hz), 4.52 (2H, t, J5.3Hz), 5.00 (1H, d, J17.5Hz), 5.29 (1H, d, J10.7Hz), 5.68 (2H, m), 6.77 (1H, dd, J17.5, 10.6Hz), 7.20 (1H, dd, J7.5, 5.3Hz), 7.29 (1H, m) 7.67 (1H, s), 8.55 (1H, d, J4.5Hz); MS (EI) *m/z* 468 (M^+), (NH_3 DCI) *m/z* 469 (MH^+), Found: 468.2991, $C_{28}H_{40}N_2O_4$ requires 468.2988.

Step 2. Mutilin 14-(*N*-2-pyridylmethyl)-carbamate

The product from step 1, (398 mg) in dioxan (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (2 ml), as for Example 1 Step 2, to afford the title compound, (184 mg, 48%); ν_{max} (CH_2Cl_2) 3445, 1732, 1713 cm^{-1}; ^1H NMR ($CDCl_3$) 0.75 (3H, d, J6.0Hz), 0.86 (3H, d, J7.0Hz), 1.1 (1H, m), 1.17 (3H, s), 1.42 (3H, s), 1.43 (4H, m), 1.71 (4H, m), 2.04 (2H, m), 2.21 (2H, m), 2.37 (1H, quintet, J6.8Hz), 3.35 (1H, dd, J10.8, 6.7Hz), 4.48 (2H, m), 5.20 (1H, dd, J17.4, 1.5Hz), 5.34 (1H, d, J11.1Hz), 5.68 (2H, includes 1H d, J8.4Hz), 6.59 (1H, dd, J17.4, 11.0Hz), 7.20 (2H, m), 7.62 (1H, td, J7.6, 1.7Hz), 8.53 (1H, d, J4.3Hz); MS (EI) *m/z* 455 (MH^+), (NH_3 DCI) *m/z* 455 (MH^+), Found: 454.2833, $C_{27}H_{38}N_2O_4$ requires 454.2832.

Example 127. (E)-Mutilin 14-[*N*-3-(1-methyl-1,2,3-triazol-4-yl)acryloyl]-carbamate

Step 1 : Methyl-(E)-3-(1-methyl-1,2,3-triazol-4-yl)acrylate

1-Methyl-1,2,3-triazol-4-carboxaldehyde (1 g, 9 mmol) was added to a solution of methoxycarbonylmethylene triphenylphosphorane (4.5 g, 13.5 mmol) in dichloromethane (50 ml) and stirred at room temperture for 3.5 hours. The solvent was removed and the residue purified by silica gel chromatography to afford the title compound, (3.2 g).

Step 2 : (E)-3-(1-Methyl-1,2,3-triazol-4-yl)acrylic acid

10% Sodium hydroxide solution (3 ml) was added to a solution of the product from step 1 (3.2 g). The mixture was stirred at room temperature for 15 hours, further 10% sodium hydroxide solution (2 ml) added and then heated to reflux for 3 hours. On cooling the reaction mixture was partitioned between ethyl acetate and water. The organics were re-extracted with saturated sodium hydrogen carbonate solution and the combined aqueous extracts acidified to pH 1 with conc. hydrochloric acid. After extraction into ethyl acetate and dying over magnesium sulphate the solvent was removed to afford the title compound, (748 mg); ^{1}H NMR (d^6-DMSO) 4.07 (3H, s), 6.53 (1H, d, J16.0Hz), 7.53 (1H, d, J16.0Hz), 8.44 (1H, s), 12.48 (1H, br).

Step 3 : (E)-(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-3-(1-methyl-1,2,3-triazol-4-yl)acryloyl]-carbamate

(E)-3-(1-Methyl-1,2,3-triazol-4-yl)acrylic acid (306 mg, 2 mmol) in dichloromethane (10 ml) was treated with oxalyl chloride (0.35 ml, 4 mmol) and one drop of DMF at room temperature for 2h. The solvent and excess oxalyl chloride were removed *in vacuo*. The residue was dissolved in toluene and the solvent again removed *in vacuo*.

The crude acid chloride was disolved in dry dichloromethane (10 ml) and treated with silver cyanate (450 mg, 3 mmol) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (335 mg, 1 mmol). After stirring at room temperature for 1.5h the title compound was isolated by the procedure described in Example 31, Step 2, (310 mg, 60%); ν_{max} (CH_2Cl_2) 3388, 1775, 1748 and 1691 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.86 (3H, d, J6.8Hz), 1.00 (3H, d, J6.4Hz), 1.07-1.55 (6H, m), 1.21 (3H, s), 1.24 (3H, s), 1.67 (1H, d, J15.5Hz), 1.73 (1H, d, J11.5Hz), 2.02 (2H, m), 2.20 (1H, m), 2.50 (1H, dd, J15.3, 10.1Hz), 2.89 (1H, q, J6.3Hz), 3.23 (3H, s), 3.46 (1H, m), 4.15 (3H, s), 5.03 (1H, d, J17.5Hz), 5.34 (1H, d, J10.7Hz), 5.76 (1H, d, J9.9Hz), 6.69 (1H, dd, J17.5, 10.7Hz), 7.62 (1H, s), 7.65 (1H, d, J15.5Hz) 7.76 (1H, s), 7.84 (1H, d, J15.7Hz); MS (NH_3 DCI) *m/z* 513 (MH^+).

Step 4 : (E)-Mutilin 14-[*N*-3-(1-methyl-1,2,3-triazol-4-yl)acryloyl]-carbamate.

The product from step 3, (272 mg) in dioxan (2 ml) was treated with a saturated solution of zinc chloride in conc. HCl (1 ml), as for Example 1 Step 2, to afford the title compound, (173 mg, 65%); ν_{max} (CH_2Cl_2) 3390, 1777, 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.76 (3H, d, J6.6Hz), 0.89 (3H, d, J7.0Hz), 1.18 (3H, s), 1.19

(1H, m), 1.45 (3H, s), 1.46 (3H, m), 1.57-1.81 (2H, m), 1.62 (3H, s), 2.05-2.36 (5H, m), 3.37 (1H, dd, J10.7, 6.6Hz), 4.14 (3H, s), 5.24 (1H, dd, J17.4, 1.3Hz), 5.40 (1H, dd, J11.1, 1.3Hz), 5.75 (1H d, J8.4Hz), 6.53 (1H, dd, J17.3, 11.0Hz), 7.54 (1H, s), 7.60 (1H, d, J15.7Hz), 7.74 (1H, s), 7.81 (1H, d; J15.7Hz); MS (EI) *m/z* 498 (M^+), (NH_3 DCI) *m/z* 516 (MH_4^+), 499 (MH^+), Found: 498.2844, $C_{27}H_{38}N_4O_5$ requires 498.2842.

Example 128. Mutilin 14-*N*-{[2-(*N*,*N*-Diethylamino)-ethylthio]-acetyl}-carbamate Hydrochloride

Mutilin 14-*N*-{[2-(*N*,*N*-diethylamino)ethylthio]acetyl}carbamate (110mg, 0.2 mmol) in methanol (4 ml) was treated with chlorotrimethylsilane (0.1 ml) and the mixture was left to stand for 10 min. The solvents were removed. Chloroform was added and removed (x2). The residue was triturated under diethyl ether, and the resultant solid was isolated by filtration and then dried over P_2O_5 *in vacuo* to give the title compound (70 mg, 59%), ν_{max} (KBr) 2926, 2674, 1770, 1728, 1512, 1506, 1453, and 1215 cm^{-1} ; ^1H NMR [$(CD_3)_2SO$] 0.65 (3H, d, *J* 6.3 Hz), 0.82 (3H, d, *J* 6.7 Hz), 1.08 (4H, s at 1.07 superposed on m), 1.15 - 1.80 (*ca.* 16H, m including t, *J* 7.2 Hz at 1.20 and s at 1.40), 2.0 - 2.3 (*ca.* 3H, m), 2.41 (1H, br s), 2.95 - 3.00 (2H, m), 3.05 - 3.18 (4H, m), 3.18 - 3.30 (2H, m), 3.46 (1H, br t; d, *J* 5.4 after D_2O exch.), 3.52 (2H, s), 4.57 (1H, d, *J* 6.0 Hz, exch D_2O), 5.04 - 5.15 (2H, m), 5.49 (1H, d, *J* 8.0 Hz), 6.21 (1H, dd, *J* 10.4, 17.7 Hz), 9.98 (1H, br s, exch D_2O), and 10.64 (1H, s, exch D_2O).

Example 129. Mutilin 14-*N*-(Formyloxy-acetyl)-carbamate

Mutilin 14-*N*-(chloroacetyl)carbamate (110 mg, 0.25 mmol) and potassium iodide (332 mg) in *N*,*N*-dimethyl-formamide (4 ml) was stirred for 10 minutes and then treated with sodium formate (68 mg), followed by more *N*,*N*-dimethylformamide (1 ml). The mixture was stirred for four days and then ethyl acetate and water were added, and the aqueous layer was re-extracted with ethyl acetate. The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel eluting with ethyl acetate hexane mixtures to give, after evaporation of requisite fractions, the title compound (120 mg, quantitative), ν_{max} (CH_2Cl_2) 3564, 3381, 2944, 1791(w), 1755 (sh), 1739, 1724, 1472, 1393, 1214, 1160, 1116, 1016, 978, and 936 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.74 (3H, d, *J* 6.9 Hz), 0.90 (3H, d, *J* 7.0 Hz), 1.20 (s), 1.42 (s), 3.37 (1H, dd, *J* 6.6, 10.6 Hz), 5.12 and 5.21 (2H, ABq *J* 17.2 Hz), 5.24 (1H, dd, *J* 1.4, 17.5 Hz), 5.38 (1H, dd, *J* 1.3, 11.1 Hz), 5.69 (1H, d, *J* 8.5 Hz), 6.45

(1H, dd, *J* 11.1, 17.4 Hz), 7.67 (1H, br s), 8.06 (1H, s); MS(CI) *m/z* 467 (MNH_4^+).

Example 130. Mutilin 14-*N*-(Hydroxyacetyl)-carbamate

Mutilin 14-*N*-(formyloxyacetyl)carbamate (140 mg, 0.31 mmol) in methanol (5 ml) was stirred for 78 h and the methanol was then removed. Chromatography of the residue on silica gel, eluting with ethyl acetate / hexane mixtures gave the title compound as a solid (58 mg, 44%), ν_{max} (CH_2Cl_2) 3564, 3386, 2932, 1786(w), 1756, 1735, 1712,1472, and 1209 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.8 Hz), 0.89 (3H, d, *J* 7.1 Hz), 1.19 (s), 1.42 (s), 2.99 (1H, t, *J* 4.9 Hz), 3.37 (1H, dd, *J* 6.6, 10.6 Hz), 4.4 - 4.6 (2H, m), 5.22 (1H, dd, *J* 1.4, 17.5 Hz), 5.37 (1H, dd, *J* 1.3, 11.1 Hz), 5.71 (1H, d, *J* 8.5 Hz), 6.45 (1H, dd, *J* 11.0, 17.4 Hz), 7.81 (1H, br s); MS(ES+) *m/z* 534$(M-H+TFA)^+$; MS(ES-) *m/z* 420 $(M-H)^-$.

Example 131. Mutilin 14-*N*-(Iodoacetyl)-carbamate

Mutilin 14-*N*-(chloroacetyl)carbamate (400 mg, 0.91 mmol) in acetone (50 ml) was treated with potassium iodide (1.2 g, 7.2 mmol), and the mixture was stirred at room temperature for 5 days. Water and ethyl acetates were added and the layers were separated. The ethyl acetate layer was washed with brine, dried ($MgSO_4$) and evaporated. The crude product was chromatographed on silica gel, eluting with ethyl acetate / hexane mixtures to give the title compound (475 mg, 86%), ^1H NMR ($CDCl_3$) 0.77 (3H, d, *J* 6.7 Hz), 0.90 (3H, d, *J* 7.0 Hz), 1.0 - 1.3 (4H, m, including s at 1.20), 1.3 - 1.9 (12H, m, including s at 1.42), 2.0 - 2.4 (4H, m), 3.37 (1H, dd, *J* 6.6, 10.5 Hz), 4.18 and 4.32 (2H, ABq *J* 9.6 Hz), 5.24 (1H, dd, *J* 1.4, 17.4 Hz), 5.39 (1H, dd, *J* 1.3, 10.9 Hz), 5.74 (1H, d, *J* 8.5 Hz), 6.48 (1H, dd, *J* 11.0, 17.4 Hz), 7.47 (1H, s).

Example 132. Mutilin 14-*N*-(Azidoacetyl)-carbamate

Mutilin 14-*N*-(iodoacetyl)carbamate (133 mg, 0.25 mmol) and sodium azide (16 mg, 0.25 mmol) were stirred together in *N,N*-dimethyl-formamide for 24h. Ethyl acetate and water were added and the layers separated. The aqueous layer was re-extracted with ethyl acetate and combined ethyl acetate layers were washed with brine, dried ($MgSO_4$) and evaporated. Chromatography on silica gel, eluting with ethyl acetate / hexane 6:4, and evaporation of requisite fractions, gave the title compound (101 mg, 90%), ν_{max} (CH_2Cl_2) 3381, 2931, 2111, 1789(w), 1755, 1724, 1470, and 1206 cm^{-1}; ^1H NMR ($CDCl_3$) 0.73 (3H, d, *J* 6.7 Hz), 0.89 (3H,

d, *J* 7.0 Hz), 1.0 - 1.3 (4H, m, including s at 1.19), 1.3 - 1.9 (12H, m, including s at 1.43), 2.0 - 2.4 (4H, m), 3.36 (1H, dd, *J* 6.6, 10.6 Hz), 4.31 and 4.40 (2H, ABq *J* 18.3 Hz), 5.23 (1H, dd, *J* 1.4, 17.4 Hz), 5.37 (1H, dd, *J* 1.3, 11.1 Hz), 5.69 (1H, d, *J* 8.5 Hz), 6.45 (1H, dd, *J* 11.0, 17.4 Hz), 7.72 (1H, s); MS(ES-) *m/z* 445 ($M-H^-$).

Example 133. Mutilin 14-*N*-[2-(3-Hydroxypyrid-2-ylthio)-acetyl]-carbamate

Mutilin 14-*N*-(chloroacetyl)carbamate (110 mg, 0.25 mmol) in *N,N*-dimethylformamide (4 ml) was treated with potassium iodide (166 mg, 1 mmol). After 10 min 3-hydroxy-2-mercaptopyridine (35 mg, 0.275 mmol) and potassium carbonate (35 mg, 0.25 mmol) and *N,N*-dimethylformamide (1ml) were added. The mixture was stirred for 24 h and then added to ethyl acetate / water. After separation the aqueous layer was re-extracted with ethyl acetate. The combined ethyl acetate layers were dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel, eluting with ethyl acetate / hexane mixtures to yield the title compound (110 mg, 83%); ν_{max} (KBr) 2956, 1782, 1725, 1711, 1523, 1491, 1449, and 1299 cm^{-1}; ^1H NMR [$(CD_3)_2SO$] 0.66 (3H, d, *J* 6.1 Hz), 0.82 (3H, d, *J* 6.7 Hz), 0.9 - 1.8 (*ca* 15 H, m, including s at 1.14 and s at 1.39), 2.0 - 2.3 (4H, m), 2.41 (1H, br s), 3.44 (1H, br t, d, *J* 5.4 Hz after D_2O exch), 4.04 (2H, s), 4.53 (1, d *J* 6.0 Hz, exch D_2O) 5.04 - 5.15 (2H,m), 5.50 (1H, d, *J* 7.9 Hz), 6.22 (1H, dd, *J* 11.1, 17.7 Hz), 6.94 - 7.06 (2H, m), 7.83 (1H, dd *J* 1.4 and 4.6 Hz), 10.43 (1H, br s, exch. D_2O), 10.65 (1H, s, exch. D_2O); MS(CI) *m/z* 531 $(M+H)^+$.

Example 134. Mutilin 14-*N*-[2-(4-Methylpyrimidin-2-ylthio)-acetyl]-carbamate

Using a simliar procedure to that described in Example 133, 2-mercapto-4-methylpyrimidine (42 mg, 0.26 mmol) was converted over 3 days into the title compound (95 mg, 71%), ν_{max} (CH_2Cl_2) 3377, 3179, 2961,1782(w), 1734, 1576, 1545, 1332, 1217, 1116, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.61 (3H, d, *J* 6.5 Hz), 0.87 (3H, d, *J* 7.0 Hz), 1.19 (s , 1.43 (s), 2.51 (3H, s), 3.34 (1H, dd, *J* 6.6, 11.1 Hz), 3.84 and 3.92 (2H, ABq *J* 15.1 Hz), 5.22 (1H, dd, *J* 1.4, 17.3 Hz), 5.37 (1H, dd, *J* 1.4, 10.9 Hz), 5.71 (1H, d, *J* 8.5 Hz), 6.54 (1H, dd, *J* 11.0, 17.4 Hz), 6.96 (1H, d *J* 5.1 Hz), 8.41 (1H, d *J* 5.2 Hz), 9.57 (1H, br s) ; MS(EI) *m/z* 589 (M^+); Found: 529.2607, $C_{28}H_{39}N_3O_5S$ requires 529.2610.

Example 135. Mutilin 14-*N*-[2-(1-Oxopyrid-2-ylthio)-acetyl]-carbamate

Using a simliar procedure to that described in Example 133, 2-mercaptopyridine-1-oxide (32 mg, 0.25 mmol) was converted in 3 days into the title compound (87 mg, 65%), ν_{max} (CH_2Cl_2) 3386, 2962, 2932,1783, 1734, 1484, 1204, 1116, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.72 (3H, d, *J* 6.7 Hz), 0.89 (3H, d, *J* 7.0 Hz), 1.18 (s), 1.42 (s),,3.36 (1H, dd, *J* 6.6, 10.5 Hz), 4.06 (2H, s), 5.24 (1H, dd, *J* 1.3, 17.4 Hz), 5.41 (1H, dd, *J* 1.3, 11.0 Hz), 5.73 (1H, d, *J* 8.4 Hz), 6.50 (1H, dd, *J* 11.0, 17.4 Hz), 7.3 (1H, dt *J* 1.7, 6.5 Hz), 7.27 (1H, dt, *J ca.* 1.2, 8 Hz) 7.51 (1H, dd *J* 1.7, 8.2 Hz), 8.27 (1H, dd, *J* 0.9, 6.4), 8.36 (1H, br s) ; MS(CI) *m/z* 531 $(MH)^+$.

Example 136. Mutilin 14-*N*-(Ethylthio-acetyl)-carbamate

Using a simliar procedure to that described in Example 133, the chloroacetyl compound (280 mg, 0.64 mmol) and sodium ethane thiolate (79 mg), with no potassium carbonate, was converted in 26 hours into the title compound (194 mg, 65%), ν_{max} (CH_2Cl_2) 3386, 2962, 2932,1782, 1756 (sh),1734, 1716 (sh), 1484, 1204, 1116, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.76 (3H, d, *J* 6.7 Hz), 0.89 (3H, d, *J* 7.1 Hz), 1.18 (s), 1.26 (t, *J* 7.4 Hz), 1.44 (s), 2.56 (2H, q, *J* 7.4 Hz), 3.36 (1H, dd, *J* 6.6, 11.7 Hz), 3.51 and 3.60 (2H, ABq, *J* 15.2 Hz), 5.22 (1H, dd, *J* 1.5, 17.4 Hz), 5.38 (1H, dd, *J* 1.4, 10.9 Hz), 5.73 (1H, d, *J* 8.5 Hz), 6.51 (1H, dd, *J* 11.0, 17.3 Hz), 7.95 (1H, br s); MS(CI) *m/z* 483 $(MNH_4)^+$.

Example 137. Mutilin 14-*N*-(Ethylsulfinyl-acetyl)-carbamate

Mutilin 14-*N*-(ethylthio-acetyl)carbamate (74 mg, 0.16 mmol) in dichloromethane (4 ml) was cooled in an ice-bath and treated with *m*-chloro-perbenzoic acid (55% pure, 50 mg, 0.16 mmol) and the mixture was stirred for 2 h. The mixture was diluted with dichloromethane and washed with aqueous $NaHCO_3$, dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel, eluting with ethyl acetate / hexane mixtures to give the title compound as a mixture of diasteroisomeric sulphoxides (57 mg, 73%), ν_{max} (CH_2Cl_2) 3380, 2940, 2932,1781, 1735, 1518, 1470, 1211, 1116, 1014, and 910 cm^{-1}; MS(ES-) *m/z* 480 $(M-H)^-$.

Example 138. Mutilin 14-*N*-(Ethylsulfonyl-acetyl)-carbamate

The Mutilin 14-*N*-(ethylthio-acetyl)carbamate (74 mg, 0.16 mmol) in dichloromethane (4 ml) was cooled in an ice-bath and treated with *m*-chloro-perbenzoic acid (55% pure, 100 mg, 0.32 mmol) and the mixture was stirred for 2 h. The mixture was diluted with dichloromethane and washed with dilute aqueous $NaHCO_3$ dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel, eluting with ethyl acetate / hexane mixtures to give the title compound (36 mg, 45%), ν_{max} (CH_2Cl_2) 3373, 2944, 1787, 1757, 1733, 1706, 1469, 1324, 1208, 1153, 1116, 1016, 939, and 910 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.75 (3H, d, *J* 6.8 Hz), 0.89 (3H, d, *J* 7.0 Hz), 1.18 (s), 3.25 (2H, q, *J* 7.5 Hz), 3.37 (1H, dd, *J* 6.7, 9.8 Hz), 4.50 (2H, br ABq), 5.24 (1H, dd, *J* 1.3, 17.3 Hz), 5.37 (1H, dd, *J* 1.3, 10.9 Hz), 5.71 (1H, d, *J* 8.4 Hz), 6.47 (1H, dd, *J* 11.1, 17.4 Hz), 8.19 (1H, br s); MS(ES-) *m/z* 496 $(M-H)^-$.

Example 139. Mutilin 14-*N*-[tert-Butyloxycarbonylmethylthio-acetyl]-carbamate

Mutilin 14-*N*-(chloroacetyl)carbamate (55 mg, 0.125 mmol) in *N,N*-dimethyl-formamide (2 ml) was treated with potassium iodide (84 mg, 0.5 mmol)and potassium carbonate (18 mg, 0.125 mmol). *tert*-Butyl 2-mercaptoacetate (18.5 mg, 0.125 mmol) in *N,N*-dimethyl-formamide (0.5 ml) was then added.. The mixture was shaken for 17 h and then treated with ethyl acetate (5 ml) / water (7.5 ml). After separation the ethyl acetate layer was washed with 1M NaOH and dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel, eluting with ethyl acetate / hexane mixtures to yield the title compound (44 mg, 63%), ^1H NMR ($CDCl_3$) *inter alia* 0.76 (3H, d, *J* 6.7 Hz), 0.88 (3H, d, *J* 7.0 Hz), 1.18 (s), 1.44 (s), 1.47 (s), 3.26 (2H, s), 3.36 (1H, dd, *J* 6.6, 10.8 Hz), 3.64 (2H, br s), 5.22 (1H, dd, *J* 1.4, 17.3 Hz), 5.37 (1H, dd, *J* 1.3, 11.0 Hz), 5.71 (1H, d, *J* 8.4 Hz), 6.51 (1H, dd, *J* 11.0, 17.3 Hz), 8.35 (1H, br s).

Example 140. Mutilin 14-*N*-[2-(Ethyloxycarbonyl)ethylthio-acetyl]-carbamate

Using the process described in Example 139 mutilin 14-*N*-(chloroacetyl)-carbamate (55 mg, 0.125 mmol) and ethyl 3-mercaptopropionate (16.8 mg, 0.125 mmol) were converted into the title compound (51 mg, 75%), ^1H NMR ($CDCl_3$) *inter alia* 0.75 (3H, d, *J* 6.7 Hz), 0.88 (3H, d, *J* 7.0 Hz), 1.19 (s), 1.26 (t, *J* 7.2 Hz), 1.44 (s), 2.62 (2H, t, *J* 6.8 Hz), 2.84 (2H, t, *J* 6.7 Hz), 3.36 (1H, dd, *J* 6.6,

10.6 Hz), 3.56 and 3.64 (2H, ABq, *J* 15.0 Hz), 5.22 (1H, dd, *J* 1.4, 17.3 Hz), 5.37 (1H, dd, *J* 1.3, 11.0 Hz), 5.71 (1H, d, *J* 8.4 Hz), 6.48 (1H, dd, *J* 11.0, 17.3 Hz), 7.90 (1H, br s).

Example 141. Mutilin 14-*N*-[(5-Methyl-1,3,4-thiadiazol-2-ylthio)-acetyl]-carbamate

Using the process described in Example 139 mutilin 14-*N*-(chloroacetyl)-carbamate (55 mg, 0.125 mmol) and 2-mercapto-5-methyl-1,3,4-thiadiazole (16.5 mg, 0.125 mmol) were converted into the title compound (38 mg, 56%), ^{1}H NMR ($CDCl_3$) *inter alia* 0.65 (3H, d, *J* 6.7 Hz), 0.88 (3H, d, *J* 7.0 Hz), 1.18 (s), 1.42 (s), 2.74 (s, 3H), 3.35 (1H, dd, *J* 6.6, 10.9 Hz), 4.14 and 4.33 (2H, ABq, *J* 15.5 Hz), 5.22 (1H, dd, *J* 1.4, 17.3 Hz), 5.38 (1H, dd, *J* 1.4, 11.0 Hz), 5.70 (1H, d, *J* 8.4 Hz), 6.53 (1H, dd, *J* 11.0, 17.3 Hz), 9.05 (1H, br s).

Example 142. Mutilin 14-*N*-[(1-Methyltetrazol-5-ylthio)-acetyl]-carbamate

Using the process described in Example 139 mutilin 14-*N*-(chloroacetyl)-carbamate (55 mg, 0.125 mmol) and 5-mercapto-1-methyl-tetrazole (14.5 mg, 0.125 mmol) were converted into the title compound (28 mg, 43%), ^{1}H NMR ($CDCl_3$) *inter alia* 0.71 (3H, d, *J* 6.7 Hz), 0.89 (3H, d, *J* 6.9 Hz), 1.19 (s), 1.41 (s), 3.36 (1H, dd, *J* 6.6, 10.7 Hz), 3.98 (3H, s), 4.46 and 4.54 (2H, ABq, *J* 16.8 Hz), 5.24 (1H, dd, *J* 1.4, 17.4 Hz), 5.39 (1H, dd, *J* 1.3, 11.1 Hz), 5.71 (1H, d, *J* 8.4 Hz), 6.49 (1H, dd, *J* 11.0, 17.3 Hz), 8.44 (1H, br s).

Example 143. Mutilin 14-*N*-[(1-Phenyl-tetrazol-5-ylthio)-acetyl]-carbamate

Using the process described in Example 139 mutilin 14-*N*-(chloroacetyl)-carbamate (55 mg, 0.125 mmol) and 5-mercapto-1-phenyl-tetrazole (22.3 mg, 0.125 mmol) were converted into the title compound, (60 mg, 82%), ^{1}H NMR ($CDCl_3$) *inter alia* 0.72 (3H, d, *J* 6.7 Hz), 0.89 (3H, d, *J* 7.0 Hz), 1.20 (s), 1.44 (s), 3.37 (1H, dd, *J* 6.6, 10.8 Hz), 4.50 and 4.60 (2H, ABq, *J* 16.6 Hz), 5.24 (1H, dd, *J* 1.4, 17.4 Hz), 5.38 (1H, dd, *J* 1.3, 11.0 Hz), 5.73 (1H, d, *J* 8.7 Hz), 6.50 (1H, dd, *J* 11.0, 17.4 Hz), 7.58 (5H, s), 8.39 (1H, br s).

Example 144. Mutilin 14-*N*-[(1,3,4-Thiadiazol-2-ylthio)-acetyl]-carbamate

Using the process described in Example 139 mutilin 14-*N*-(chloroacetyl)-carbamate (55 mg, 0.125 mmol) and 2-mercapto-1,3,4-thiadiazole (14.9 mg, 0.125 mmol) were converted into the title compound (37 mg, 60%), ^{1}H NMR ($CDCl_3$) *inter alia* 0.67 (3H, d, *J* 6.7 Hz), 0.88 (3H, d, *J* 6.9 Hz), 1.19 (s), 1.42 (s),3.36 (1H, dd, *J* 6.5, 10.9 Hz), 4.29 and 4.47 (2H, ABq, *J* 15.8 Hz), 5.24 (1H, d, *J* 17.3 Hz), 5.38 (1H, d, *J* 12.0 Hz), 5.70 (1H, d, *J* 8.4 Hz), 6.51 (1H, dd, *J* 11.0, 17.4 Hz), 8.77 (1H, br s), 9.13 (1H, s).

Example 145. Mutilin 14-*N*-[(5-Aminocarbonyl-1,3,4-thiadiazol-2-ylthio)-acetyl]-carbamate

Using the process described in Example 139 mutilin 14-*N*-(chloroacetyl)-carbamate (55 mg, 0.125 mmol) and 2-mercapto-1,3,4-thiadiazole-5-carbamate (16.1 mg, 0.125 mmol) were converted into the title compound (21 mg, 29%), ^{1}H NMR ($CDCl_3$) *inter alia* 0.67 (3H, d, *J* 6.7 Hz), 0.88 (3H, d, *J* 7.0 Hz), 1.19 (s), 1.42 (s), 3.36 (1H, dd, *J* 6.5, 10.8 Hz), 4.29 and 4.47 (2H, ABq, *J* 15.8 Hz), 5.24 (1H, d, *J* 17.5 Hz), 5.39 (1H, d, *J* 10.9 Hz), 5.71 (1H, d, *J* 8.4 Hz), 5.86 (1H, s), 6.51 (1H, dd, *J* 11.0, 17.3 Hz), 7.10 (1H, s), 8.48 (1H, br s).

Example 146. Mutilin 14-*N*-[(5-Aminocarbonyl-1,3,4-oxadiazol-2-ylthio)-acetyl]-carbamate

Using the process described in Example 139 mutilin 14-*N*-(chloroacetyl)-carbamate (55 mg, 0.125 mmol) and 2-mercapto-1,3,4-oxadiazole-5-carbamate (20.1 mg, 0.125 mmol) were converted into the title compound (8 mg, 11%), ^{1}H NMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.8 Hz), 0.90 (3H, d, *J* 6.8 Hz), 1.19 (s), 1.43 (s),3.37 (1H, dd), 4.54 and 4.61 (2H, ABq, *J* 17.0 Hz), 5.25 (1H, dd, *J* 1.3, 17.4 Hz), 5.39 (1H, dd, *J* 1.2, 11.0 Hz), 5.72 (1H, d, *J* 8.4 Hz), 6.01 (1H, br s), 6.48 (1H, dd, *J* 11.1, 17.4 Hz), 7.01 (1H, br s), 8.21 (1H, br s).

Example 147. Mutilin 14-*N*-[1-(2-Dimethylaminoethyl)-tetrazol-5-ylthio]-acetyl}-carbamate

Mutilin 14-*N*-(iodoacetyl)carbamate (133 mg, 0.25 mmol) in *N,N*-dimethyl-formamide (2 ml) was treated with potassium carbonate (35 mg, 0.25 mmol) and 1-(2-dimethylaminoethyl)-5-mercaptotetrazole (43 mg, 0.25 mmol). The mixture

was shaken for 17 h and then treated with ethyl acetate (5 ml) / water (5 ml). After separation the aqueous layer was re-extracted with ethyl acetate (5 ml). The combined ethyl acetate layers were washed with brine, and dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel, eluting with ethyl acetate / hexane mixtures to yield the title compound (96 mg, 66%), ν_{max} (CH_2Cl_2) 3384, 2948, 1782, 1733, 1468, 1390, 1215, 112, 1116, 1016, and 938 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.68 (3H, d, *J* 6.7 Hz), 0.87 (3H, d, *J* 7.0 Hz), 1.17 (s), 1.42 (s), 2.23 (s), 2.73 (2H, t, *J* 6.2 Hz), 3.34 (1H, dd, *J* 6.5, 10.5 Hz), 4.33 (4H, t *J* 6.1 Hz), 5.21 (1H, dd, *J* 1.3, 17.3 Hz), 5.37 (1H, dd, *J* 1.3, 11.0 Hz), 5.69 (1H, d, *J* 8.4 Hz), 6.49 (1H, dd, *J* 11.0, 17.4 Hz), 8.68 (1H, br s); MS(EI) *m/z* 576 (M^+); Found: 576.3072, $C_{28}H_{44}N_6O_5S$ req. 576.3094.

Example 148. Mutilin 14-*N*-[(1,2,3-Triazol-5-ylthio)-acetyl]-carbamate

Using the process described in Example 147 mutilin 14-*N*-(iodoacetyl)-carbamate (133 mg, 0.25 mmol) and the sodium salt of 5-mercapto-1,2,3-triazole (31mg, 0.25 mmol), in the absence of potassium carbonate, were converted into the title compound (75 mg, 55%), ν_{max} (CH_2Cl_2) 3408, 3220, 2930, 1781, 1733, 1471, 1410, 1387, 1209,1116, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.70 (3H, d, *J* 6.7 Hz), 0.87 (3H, d, *J* 7.0 Hz), 1.17 (s), 1.42 (s), 3.35 (1H, br s), 3.93 (2H, s),5.21 (1H, dd, *J* 1.3, 17.4 Hz), 5.35 (1H, dd, *J* 1.2, 11.1 Hz), 5.69 (1H, d, *J* 8.4 Hz), 6.49 (1H, dd, *J* 11.0, 17.4 Hz), 7.67 (1H, s), 8.65 (1H, br s); MS(CI) *m/z* 522 $(MNH_4)^+$.

Example 149. Mutilin 14-*N*-{[1-(Methoxycarbonylmethyl)-tetrazol-5-ylthio]-acetyl}-carbamate

Using the process described in Example 147 mutilin 14-*N*-(iodoacetyl)-carbamate (133 mg, 0.25 mmol) and methyl 5-(mercapto-tetrazol-1-yl)-acetate (44mg, 0.25 mmol) were converted into the title compound (77 mg, 53%), ν_{max} (CH_2Cl_2) 3380, 2958, 1783, 1759, 1733, 1459,1217, 1183, 1116, 1016, and 939 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.69 (3H, d, *J* 6.8 Hz), 0.87 (3H, d, *J* 7.0 Hz), 1.17 (s), 1.41 (s), 3.35 (1H, dd, *J* 6.5, 10.7 Hz), 4.46 and 4.56 (2H, ABq *J* 16.9 Hz), 5.13 (2H, s), 5.22 (1H, dd, *J* 1.3, 17.3 Hz), 5.37 (1H, dd, *J* 1.3, 11.1 Hz), 5.69 (1H, d, *J* 8.4 Hz), 6.47 (1H, dd, *J* 11.0, 17.4 Hz), 8.26 (1H, br s); MS(Cl) *m/z* 595 $(MNH_4)^+$.

Example 150. Mutilin 14-*N*-{[3-(Methoxycarbonyl)-pyrid-2-ylthio]-acetyl}-carbamate

Using the process described in Example 147 mutilin 14-*N*-(iodoacetyl)-carbamate (133 mg, 0.25 mmol) and methyl methyl 2-mercapto-pyridine-3-carboxylate (42mg, 0.25 mmol) were converted into the title compound (48 mg, 33%), ν_{max} (CH_2Cl_2) 3380, 2956, 1781, 1720, 1401, 1214, 1139, 1116, 1071, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.55 (3H, d, *J* 6.6 Hz), 0.84 (3H, d, *J* 7.0 Hz), 1.14 (s), 1.36 (s), 3.31 (1H, dd, *J* 6.6, 11.0 Hz), 3.91 (2H, s), 3.94 (3H, s), 5.19 (1H, dd, *J* 1.4, 17.3 Hz), 5.35 (1H, dd, *J* 1.4, 10.9 Hz), 5.65 (1H, d, *J* 8.5 Hz), 6.47 (1H, dd, *J* 11.0, 17.4 Hz), 7.20 (1H, dd *J* 5.0, 7.8 Hz), 8.30 (1H, dd *J* 1.8, 7.8 Hz), 8.55 (1H, dd, *J* 1.7, 4.8 Hz), 9.45 (1H, br s); MS(CI) *m/z* 573 $(MH)^+$.

Example 151. Mutilin 14-*N*-[(2-Furylmethylthio)-acetyl]-carbamate

Using the process described in Example 147 mutilin 14-*N*-(iodoacetyl)-carbamate (133 mg, 0.25 mmol) and (2-furyl)-methyl mercaptan (29 mg, 0.25 mmol) were converted into the title compound (43 mg, 53%), ν_{max} (CH_2Cl_2) 3382, 2930, 1783, 1734, 1483, 1206, 1152, 1116, 1014, and 938 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.73 (3H, d, *J* 6.6 Hz), 0.87 (3H, d, *J* 7.0 Hz), 1.18 (s), 1.42 (s), 3.35 (1H, dd, *J* 6.7, 10.7 Hz), 3.48 and 3.56 (2H, ABq *J* 15.7 Hz), 3.76 (2H, s), 5.21 (1H, dd, *J* 1.4, 17.3 Hz), 5.36 (1H, dd, *J* 1.3, 11.1 Hz), 5.70 (1H, d, *J* 8.4 Hz), 6.21 (1H, d, *J* 3.4 Hz), 6.28 (1H, *J* d 1.9, 5.01 Hz), 6.48 (1H, dd, *J* 11.0, 17.4 Hz), 7.34 (1H, dd *J* 0.8, 1.9 Hz), 7.80 (1H, br s); MS(CI) *m/z* 535 $(MNH_4)^+$.

Example 152. Mutilin 14-*N*-[(2,3-Dihydroxypropylthio)-acetyl]-carbamate

Using the process described in Example 147 mutilin 14-*N*-(iodoacetyl)-carbamate (133 mg, 0.25 mmol) and 3-mercapto-1,2-propane-diol (0.021 ml, 27 mg, 0.25 mmol) were converted into the title compound (37 mg, 28%); ν_{max} (CH_2Cl_2) 3380, 2929, 1782, 1733, 1471, 1409, 1206, 1115, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.74 (3H, d, *J* 6.5 Hz), 0.87 (3H, d, *J* 7.0 Hz), 1.17 (s), 1.42 (s), 2.56 - 2.81 (2H,m), 3.12 (1H, s, exch. D_2O), 3.35 (1H, dd, *J* 6.6, 10.5 Hz; d, *J* 6.4 after D_2O exch.), 3.50 - 3.58 (1H, m), 3.96 - 4.11 (2H, m), 4.13 - 4.21 (1H, m), 5.21 (1H, dd, *J* 1.3, 17.4 Hz), 5.36 (1H, d, *J* 11.1 Hz), 5.69 (1H, d, *J* 8.4 Hz), 6.47 (1H, dd, *J* 11.0, 17.4 Hz), 7.99 (1H, br s); MS(ES+) *m/z* 529 $(MNH_4)^+$.

Example 153. Mutilin 14-*N*-[(Pyrid-2-ylthio)-acetyl]-carbamate

Using the process described in Example 147 mutilin 14-*N*-(iodoacetyl)-carbamate (133 mg, 0.25 mmol) and 2-mercapto-pyridine (28 mg, 0.25 mmol) were converted into the title compound (107 mg, 83%), ν_{max} (CH_2Cl_2) 3557, 3379, 3151, 2932, 1779, 1733, 1584, 1527, 1456, 1417, 1220, 1152, 1116, 1034, and 1016 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.56 (3H, d, *J* 6.4 Hz), 0.84 (3H, d, *J* 7.0 Hz), 1.14 (s), 1.38 (s), 3.32 (1H, d, *J* 6.5, Hz), 3.70 and 3.84 (2H, ABq, *J* 14.5 Hz), 5.19 (1H, dd, *J* 1.5, 17.4 Hz), 5.35 (1H, dd, *J* 1.5, 10.9 Hz), 5.65 (1H, d, *J* 8.6 Hz), 6.57 (1H, dd, *J* 10.9, 17.3 Hz), 7.06 - 7.16 (1H, m), 7.24 - 7.30 (2H, m), 7.55 (1H, m), 8.42 - 8.45 (1H, m), 10.71 (1H, br s); MS(EI) *m/z* 514 (M^+); Found: 514.2485, $C_{28}H_{38}N_2O_5S$ requires 514.2501.

Example 154. Mutilin 14-*N*-[(Cyanothio)-acetyl]-carbamate

Using the process described in Example 147 mutilin 14-*N*-(iodoacetyl)-carbamate (133 mg, 0.25 mmol) and ammonium thiocyanate (19 mg, 0.25 mmol), in the absence of potassium carbonate, were converted into the title compound (105 mg, 90%), ν_{max} (CH_2Cl_2) 3376, 2931, 1752, 1735, 1721, 1472, 1216, 1188, 1116, 1016, and 939 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.72 (3H, d, *J* 6.9 Hz), 0.88 (3H, d, *J* 7.0 Hz), 1.18 (s), 1.41 (s), 3.36 (1H, dd, *J* 6.6, 10.4 Hz), 4.37 (2H, s), 5.23 (1H, dd, *J* 1.3, 17.3 Hz), 5.38 (1H, dd, *J* 1.2, 10.9 Hz), 5.68 (1H, d, *J* 8.5 Hz), 6.41 (1H, dd, *J* 11.0, 17.4 Hz), 7.94 (1H, br s); MS(ES-) *m/z* 461 $(M-H)^-$.

Example 155. Mutilin 14-*N*-[*N*-Acetylglycyl]carbamate

Mutilin 14-*N*-(azidoacetyl)carbamate (113 mg, 0.25 mmol) in dry tetrahydrofuran (1 ml) under argon was treated with tri-*n*-butylphosphine (0.045 ml, 55 mg, 0.275 mmol) and the mixture was stirred under argon for 1 h. The solution was then cooled to -50°C and acetyl chloride (0.024 ml, 21 mg, 0.275 mmol) was added. The mixture was stirred for 45 min and then saturated aqueous $NaHCO_3$ (0.5 ml) was added and the mixture was allowed to warm to room temperature. Ethyl acetate and brine were added, the layers were separated and the ethyl acetate layer was dried ($MgSO_4$)and evaporated. The residue was chromatographed on silica gel, eluting with ethyl acetate hexane mixtures to give the title compound (20 mg, 17%), ν_{max} (CH_2Cl_2) 3427, 3385, 2961, 2935, 1783, 1756, 1732, 1674, 1509, and 1474 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.71 (3H, d, *J* 6.8 Hz), 0.87 (3H, d, *J* 7.0 Hz), 1.17 (s), 1.41 (s), 2.04 (s), 2.54 (1H, br d *J* 6.0 Hz\), 4.38 and 4.47 (2H, dABq, *J* 4.9 and 19Hz), 5.21 (1H, dd, *J* 1.1, 17.3 Hz), 5.36 (1H, dd, *J* 1.1,

10.9 Hz), 5.68 (1H, d, *J* 8.4 Hz), 6.26 (1H, br t, *J ca.* 4.6 Hz), 6.46 (1H, dd, *J* 11.1, 17.4 Hz), 8.06 (1H, br s); (MS) (ES-) 461 $(M-H)^-$.

Example 156. Mutilin 14-*N*-(*N*,*N*-Diethylglycyl)carbamate

Mutilin 14-*N*-(iodoacetyl)carbamate (133 mg, 0.25 mmol) in diethylether (1.5 ml) was treated with diethylamine (0.03 ml). After 2 h and 6 h further aliquots of diethylamine (0.03 ml) were added and stirring was continued for a further 17 h. Ethyl acetate / water were added followed by 1M NaOH (2ml). The aqueous layer was re-extracted with ethyl acetate, and combined ethyl acetate layers were dried ($MgSO_4$). and evaporated. Chromatography on silica gel, eluting with ethyl acetate / hexane 6:4, and evaporation of requisite fractions gave the title compound (103 mg, 83%), MS(CI) *m/z* 477 $(MH)^+$.

Example 157. Mutilin 14-{*N*-[(1-Methyl-1,2,3-triazol-4-yl)-carbonyl]-carbamate}

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[(1-methyl-1,2,3-triazol-4-yl)carbonyl]carbamate}

1-Methyl-1,2,3-triazole-4-carboxylic acid (2.00 g) in dichloromethane (50 ml) at room temperature was treated with oxalyl chloride (2.40 g) and two drops of DMF for 3 h. IR analysis showed complete conversion to the acid chloride. The solvent and excess oxalyl chloride were removed *in vacuo* and the residue was re-evaporated from toluene to yield the acid chloride as a white solid.

The acid chloride (0.436 g), silver cyanate (0.450 g) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.334 g) were then suspended in dry dichloromethane (5 ml) and stirred at room temperature for 4 h. The resulting suspension was filtered through Celite, washing well with dichloromethane. The organic solution was washed with water, saturated sodium chloride solution and dried ($MgSO_4$). After filtration, the solvent was evaporated to yield the crude product. Purification by silica gel chromatography, eluting with ethyl acetate - hexane mixtures, provided the pure product as a colourless foam, (0.486 g); ^1H NMR ($CDCl_3$) 0.90 (3H, d, J6.9Hz), 1.00 (3H, d, J6.4Hz), 1.05-1.80 (m), 1.21 (3H, s), 1.30 (3H, s), 1.90-2.10 (2H, m), 2.14-2.28 (1H, m) 2.52 (1H, dd, J10.1,15.3Hz), 2.90 (1H, q, J6.4Hz), 3.24 (3H, s), 3.40-3.55 (1H, m), 4.20 (3H, s), 5.00 (1H, d, J17.5Hz), 5.30 (1H, d, J10.8Hz), 5.83 (1H, d, J 9.9Hz), 6.78 (1H, dd, J10.7,17.5Hz), 8.20 (1H, s) and 9.10 (1H, s).

Step 2. Mutilin 14-{*N*-[(1-Methyl-1,2,3-triazol-4-yl)carbonyl]carbamate}

The product from step 1, (0.450 g) in 1,4-dioxan (4 ml) was stirred at room temperature for 8 h with Lukas reagent (1.25 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, the title compound was isolated as a white solid, (0.405 g); ^{1}H NMR ($CDCl_3$) 0.79 (3H, d, J6.5 Hz), 0.89 (3H, d, J7.0Hz), 1.20 (3H, s), 1.40-1.90 (m), 1.52 (3H, s), 2.08-2.45 (5H, m), 3.39 (1H, dd, J6.6,11.0Hz), 4.19 (3H, 3), 5.22 (1H, dd, J1.5,17.4Hz), 5.39 (1H, dd, J1.4,10.9Hz), 5.83 (1H, d, J8.4Hz), 6.59 (1H, dd, J10.95,17.3Hz) 8.19 (1H, s) and 9.03 (1H, s); MS (NH_4 DCI) *m/z* 490 (MNH_4^+), 473 (MH^+).

Example 158. Mutilin 14-{*N*-[(1,2,3-thiadiazol-4-yl)-carbonyl]carbamate}

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[(1,2,3-thiadiazol-4-yl)- carbonyl]carbamate}

1,2,3-Thiadiazole-4-carboxylic acid was converted to the acid chloride and reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.334 g) as described for Example 157. Following purification by silica gel chromatography the title compound was obtained as a colourless foam (0.490 g); ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, J6.9Hz), 1.00 (3H, d, J6.4Hz), 1.05-1.68 (m), 1.21 (3H, s), 1.30 (3H, s), 1.7-1.82 (2H, m), 1.92-2.10 (2H, m), 2.14-2.28 (1H, m) 2.58 (1H, dd, J10.1,15.3Hz), 2.90 (1H, q, J6.3Hz), 3.25 (3H, s), 3.40-3.55 (1H, m), 5.02 (1H, d, J17.5Hz), 5.32 (1H, d, J10.0Hz), 5.89 (1H, d, J 9.9Hz), 6.77 (1H, dd, J10.6,17.5Hz), 9.42 (1H, s) and 9.43 (1H, s).

Step 2. Mutilin 14-{*N*-[(1,2,3-thiadiazol-4-yl)carbonyl]carbamate}

The product from step 1, (0.460 g) in 1,4-dioxan (4 ml) was stirred at room temperature for 7 h with Lukas reagent (1.25 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, the title compound was isolated as a white solid, (0.359 g); ^{1}H NMR ($CDCl_3$) 0.81 (3H, d, J6.7 Hz), 0.90 (3H, d, J7.0Hz), 1.20 (3H, s), 1.38-1.88 (m), 1.55 (3H, s), 2.10-2.45 (5H, m), 3.39 (1H,

dd, J6.6,10.9Hz), 5.22 (1H, dd, J1.5,17.2Hz), 5.40 (1H, dd, J1.4,11.1Hz), 5.89 (1H, d, J8.5 Hz), 6.59 (1H, dd, J11.05,17.4Hz) and 9.40 (2H, s): MS (NH_4 DCI) *m/z* 493 (MNH_4^+).

Example 159. Mutilin 14-{*N*-[(1-ethyl-5-methylpyrazol-3-yl)-carbonyl]carbamate}

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[(1-ethyl-5-methylpyrazol-3-yl)carbonyl]carbamate}

1-Ethyl-5-methylpyrazole-3-carboxylic acid was converted to the acid chloride and reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.334 g) as described for Example 157. Following purification by silica gel chromatography the title compound was obtained as a colourless foam (0.140 g); ^1H NMR ($CDCl_3$) 0.90 (3H, d, J6.9Hz), 1.00 (3H, d, J6.4Hz), 1.05-1.64 (m), 1.20 (3H, s), 1.37 (3H, s), 1.42 (3H, t, J7.3Hz), 1.71(1H, d, J5.5Hz), 1.79 (1H, s), 1.95-2.10 (2H, m), 2.12-2.29 (1H, m), 2.31 (3H, s), 2.52 (1H, dd, J10.1,15.3Hz), 2.92 (1H, q, J6.3Hz), 3.22 (3H, s), 3.40-3.55 (1H, m), 4.12 (2H, q, J7.25Hz), 5.02 (1H, d, J17.5Hz), 5.28 (1H, d, J10.7Hz), 5.83 (1H, d, J 9.9Hz), 6.63 (1H, s), 6.78 (1H, dd, J10.7,17.5Hz), and 8.88 (1H, s).

Step 2. Mutilin 14-{*N*-[(1-ethyl-5-methylpyrazol-3-yl)carbonyl]carbamate}

The product from step 1, (0.130 g) in 1,4-dioxan (3.5 ml) was stirred at room temperature for 5 h with Lukas reagent (1.0 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, the title compound was isolated as a white solid, (0.133 g); ^1H NMR ($CDCl_3$) 0.80 (3H, d, J6.5 Hz), 0.90 (3H, d, J7.0Hz), 1.19 (3H, s), 1.35-1.88 (m), 1.46 (3H, t, J7.22Hz), 1.55 (3H, s), 2.30 (3H, s), 2.05-2.45 (5H, m), 3.38 (1H, dd, J6.5,10.9Hz), 4.10 (2H, q, J7.25Hz), 5.22 (1H, dd, J1.6,17.4Hz), 5.39 (1H, dd, J1.4,10.9Hz), 5.85 (1H, d, J8.5 Hz), 6.59 (1H, dd, J11.0,17.4Hz) 6.61 (1H, s) and 8.80 (1H, s); MS (EI) *m/z* 499.

Example 160. Mutilin 14-{*N*-[(1,5-Dimethylpyrazol-3-yl)-carbonyl]carbamate}

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[(1,5-dimethylpyrazol-3-yl)carbonyl]carbamate}

1,5-Dimethylpyrazole-3-carboxylic acid was converted to the acid chloride and reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.334 g) as described for Example 157. Following purification by silica gel chromatography the title compound was obtained as a colourless foam (0.450 g); ^{1}H NMR ($CDCl_3$) 0.90 (3H, d, J6.9Hz), 1.00 (3H, d, J6.4Hz), 1.05-1.65 (m), 1.20 (3H, s), 1.35 (3H, s), 1.70(1H, d, J6.5Hz), 1.78 (1H, d, J2.2Hz), 1.95-2.10 (2H, m), 2.14-2.28 (1H, m), 2.30 (3H, s), 2.51 (1H, dd, J10.1,15.3Hz), 2.92 (1H, q, J6.3Hz), 3.22 (3H, s), 3.40-3.57 (1H, m), 3.81 (3H, s), 5.0 (1H, d, J17.2Hz), 5.29 (1H, d, J10.7Hz), 5.82 (1H, d, J 9.9Hz), 6.63 (1H, s), 6.78 (1H, dd, J10.7,17.5Hz), and 8.84 (1H, s).

Step 2. Mutilin 14-{*N*-[(1,5-dimethylpyrazol-3-yl)carbonyl]carbamate}

The product from step 1, (0.420 g) in 1,4-dioxan (4.0 ml) was stirred at room temperature for 4 h with Lukas reagent (1.4 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, the title compound was isolated as a white solid, (0.360 g); ^{1}H NMR ($CDCl_3$) 0.80 (3H, d, J6.5 Hz), 0.90 (3H, d, J7.0Hz), 1.19 (3H, s), 1.32-1.88 (m), 1.55 (3H, s), 2.29 (3H, s), 2.05-2.45 (5H, m), 3.39 (1H, dd, J6.5,10.9Hz), 3.80 (3H, s), 5.22 (1H, dd, J1.6,17.4Hz), 5.39 (1H, dd, J1.4,10.9Hz), 5.82 (1H, d, J8.5 Hz), 6.60 (1H, dd, J11.0,17.4Hz) 6.62 (1H, s) and 8.79 (1H, s); MS (EI) *m/z* 485.

Example 161. Mutilin 14-[*N*-(*N*-Methylnipecotyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(*N*-methylnipecotyl)carbamate]

(±)-Ethyl *N*-methylnipecotate (5.0 g) was dissolved in 5M hydrochloric acid (100 ml) and stirred at room temperature for 16 h. The solution was then evaporated at reduced pressure and the residue re-evaporated from toluene (x2). Trituration gave the hydrochloride salt of (±)-*N*-methylnipecotic acid as a white solid (3.91 g).

The hydrochloride salt of (±)-*N*-methylnipecotic acid (1.0 g) was suspended in dichloromethane (25 ml) and stirred at room temperature for 2 h with oxalyl chloride (0.58 ml) and DMF (1 drop). The solvent was then evaporated to yield the hydrochloride salt of *N*-methylnipecotyl chloride as a pale yellow solid.

The above acid chloride (0.596 g) was suspended in dry dichloromethane and stirred at room temperature for 4 h with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.334 g), silver cyanate (0.450 g) and triethylamine (0.276 ml). The suspension was then filtered through Celite, diluted with ethyl acetate and washed with water and saturated sodium chloride solution. The organic solution was dried (MgSO4), filtered and evaporated to yield the crude product. Silica gel column chromatography, eluting with a gradient of 0-5% 9:1 methanol/ 35% ammonia solution in dichloromethane gave the title compound as a diastereomeric mixture and as a colourless oil (0.290 g); ^{1}H NMR ($CDCl_3$) 0.85 and 0.88 (2xd, all 3H, J6.9Hz), 1.00 (3H, d, J6.4Hz), 1.05-1.85 (m), 1.20 (3H, s), 1.25 (3H, s), 1.9-2.40 (6H, m), 2.32 (3H, 2xs), 2.48 (1H, m), 2.69(1H, broad res.), 2.80-2.98 (3H, broad q,), 3.22 (3H, s), 3.40-3.53 (1H, m), 4.98 (1H, d, J17.6Hz), 5.29 (1H, d, J10.7Hz), 5.62-5.72 (1H, 2xd, J9.9Hz) and 6.78-6.91 (1H,m); MS (EI) *m/z* 503.

Step 2. Mutilin 14-[*N*-(*N*-Methylnipecotyl)carbamate]

The product from step 1, (0.250 g) in 1,4-dioxan (3.0 ml) was stirred at room temperature for 4 h with conc. hydrochloric acid (2.0 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, eluting with a gradient of 0-5% 9:1 methanol/35% ammonia solution in dichloromethane, the title compound was isolated as a diastereoisomeric mixture and as a white foam, (0.205 g); ^{1}H NMR ($CDCl_3$) 0.78 (3H, 2xd, J6.7 Hz), 0.89 (3H, d, J7.0Hz), 1.19 (3H, s), 1.35-2.40 (m), 1.47 (3H, s), 2.30 (3H, 2xs),2.63-2.90 (2H, broad res.), 3.35 (1H, broad res.), 5.22 (1H, d, J17.4Hz), 5.39 (1H, dd, J1.4,11.0Hz), 5.60-5.72 (1H, 2xd, J8.5 Hz), and 6.63 (1H, dd, J11.0,17.4Hz); MS (EI) *m/z* 488.

Example 162. Mutilin 14-[*N*-(1-Methylpyrrolidin-3-oyl)-carbamate]

Step 1. 3-Ethoxycarbonyl-1-methylpyrrolidin-2-one

1-Methyl-2-pyrrolidinone (9.9 g) and diethyl carbonate (50 g) were dissolved in toluene and refluxed for 1 h with the provison for the removal of water (Dean and Stark apparatus). After cooling, sodium hydride (50% dispersion in oil; 8.53 g) was carefully added and the stirred suspension was heated to reflux for 4 h under an atmosphere of argon. After cooling, acetic acid (15 ml) was added and the suspension was filtered. The filtrate was evaporated and the residue chromatographed over silics gel to yield the desired product as a colourless oil (5.9 g); ^{1}H NMR ($CDCl_3$) 1.30 (3H, t), 2.18-2.50 (2H, m), 2.88 (3H, s), 3.3-3.59 (3H, m), 4.25 (2H, t).

Step 2. 3-Ethoxycarbonyl-1-methylpyrrolidine

The product from step 1 (2.0 g) was dissolved in dry dichloromethane (MDC) and added to a solution of triethyloxonium tetrafluoroborate (2.8 g) in MDC (100 ml). The solution was stirred under argon at room temperature for 16 h., and then evaporated. The residue was dissolved in ethanol, cooled to ice-bath temperature under argon and sodium borohydride (0.889 g) was added. The resulting solution was stirred at room temperature for 16 h. Water (15 ml) was added and the solution was evaporated and re-evaporated from toluene (x2). The residue was chromatographed over silica gel, eluting with a gradient of 0-20% methanol/35% ammonia solution (9:1) in MDC, to yield the desired product as a pale yellow oil (0.450 g); MS (ES) *m/z* 158 (MH^+).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-1-methylpyrrolidin-3-oyl)carbamate]

The ethyl ester from step 2 was converted to the acid chloride by the procedure described in example 5, step 1. This acid chloride was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.668 g) according to the procedure of example 5 to yield the title compound as a diastereomeric mixture and as a pale yellow foam (0.350 g); MS (ES) *m/z* 489 (MH^+).

Step 4. Mutilin 14-[*N*-(1-Methylpyrrolidin-3-oyl)carbamate]

The product from step 3, (0.320 g) in 1,4-dioxan (4.0 ml) was stirred at room temperature for 4 h with conc. hydrochloric acid (2.0 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen

carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, eluting with a gradient of 0-5% 9:1 methanol/35% ammonia solution in dichloromethane, the title compound was isolated as a diastereoisomeric mixture and as a pale yellow foam, (0.245 g); ^1H NMR ($CDCl_3$) *inter alia* 0.75 (3H, d, J6.7 Hz), 0.89 (3H, d, J7.0Hz), 1.19 (3H, s), 1.48 (3H, s), 2.42 (3H, 2xs),2.82-3.05 (2H, broad res.), 3.37 (1H, broad res.), 5.22 (1H, d), 5.38 (1H, d) 5.60-5.72 (1H, 2xd, J8.6 Hz), and 6.50-6.65 (1H, m); MS (ES) *m/z* 475 (MH^+).

Example 163. Mutilin 14-[*N*-(1-Allylpiperidin-4-oyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-allylpiperidin-4-oyl)carbamate]

1-Allylpiperidine-4-carboxylic acid was converted to the acid chloride hydrochloride by the procedure described in Example 161. This acid chloride was then reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.334 g) by the procedure outlined in Example 161 to yield the title compound as a colourless foam (0.373 g) after silica gel column chromatography; MS (ES) *m/z* 529 (MH^+).

Step 2. Mutilin 14-[*N*-(1-Allylpiperidin-4-oyl)carbamate]

The product from Step 1, (0.340 g) in 1,4-dioxan (3.0 ml) was stirred at room temperature for 7 h with conc. hydrochloric acid (2.0 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, eluting with a gradient of 0-10% 9:1 methanol/35% ammonia solution in dichloromethane, the title compound was isolated as a white solid, (0.192 g); ^1H NMR ($CDCl_3$) 0.75 (3H, d, J6.5 Hz), 0.89 (3H, d, J7.0Hz), 1.20 (3H, s), 1.40-2.45 (m), 1.45 (3H, s), 2.90-3.10 (5H, m), 3.39 (1H, dd, J6.6,10.4Hz), 5.10-5.30 (3H, m), 5.37 (1H, dd, J1.2,10.9Hz), 5.70 (1H, d, J8.4Hz), 5.78-5.98 (1H, m), 6.50 (1H, dd, J11.10,17.4Hz) and 7.43 (1H, s); MS (ES) *m/z* 515 (MH^+).

Example 164. Mutilin 14-[*N*-(1-Cyclopropylmethylpiperidin-4-oyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-1-cyclopropylmethylpiperidin-4-oyl)carbamate]

1-Cyclopropylmethylpiperidine-4-carboxylic acid was converted to the acid chloride hydrochloride by the procedure described in Example 161. This acid chloride was then reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.334 g) by the procedure outlined in Example 161 to yield the title compound as a colourless foam (0.450 g) after silica gel column chromatography; MS (EI) *m/z* 542 (M^+).

Step 2. Mutilin 14-[*N*-(1-cyclopropylmethylpiperidin-4-oyl)carbamate]

The product from step 1, (0.400 g) in 1,4-dioxan (5.0 ml) was stirred at room temperature for 7 h with conc. hydrochloric acid (2.0 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, eluting with a gradient of 0-10% 9:1 methanol/35% ammonia solution in dichloromethane, the title compound was isolated as a white solid, (0.190 g); ^1H NMR ($CDCl_3$) 0.12 (2H,m), 0.53 (2H, m), 0.75 (3H, d, J6.5 Hz), 0.90 (3H, d, J7.0Hz), 1.20 (3H, s), 1.35-2.40 (m), 1.42 (3H, s), 2.95-3.18 (3H, m), 3.39 (1H, dd, J6.6,10.4Hz), 5.25(1H, dd, J1.4, 17.4Hz), 5.38 (1H, dd, J1.2,10.9Hz), 5.70 (1H, d, J8.4Hz), 6.50 (1H, dd, J11.10,17.4Hz) and 7.40 (1H, s); MS (EI) *m/z* 515.

Example 165. Mutilin 14-[*N*-(nipecotyl)carbamate]

Step 1. *N*-*t*-Butoxycarbonyl nipecotic acid

(±)-Nipecotic acid was dissolved in water (25 ml) and stirred rapidly at room temperature for 16 h with a solution of *t*-butoxycarbonyl anhydride (3.27 g) in 1,4-dioxan (25 ml). The solution was then evaporated to small volume, adjusted to pH 2.0 by the addition of 5M hydrochloric acid solution, and the resulting precipitate was extracted with dichloromethane. The organic solution was washed with brine, dried ($MgSO_4$) and evaporated at reduced pressure. The residue was triturated with ether/hexane and the resulting white solid collected by filtration (1.10 g); MS (EI) *m/z* 229

Step 2. Mutilin 11-dichloroacetyl-14-[*N*-(*N*-*t*-butoxycarbonyl-nipecotyl)carbamate]

The product from Step 1 (0.458 g) was converted to the acid chloride by the procedure described in Example 161. This was then dissolved in dry dochloromethane (20 ml) and stirred vigorously at room temperature for 3 days with silver cyanate (0.6 g), mutilin 11-dichloroacetate (0.432 g) and tetrakis(triphenylphosphine) palladium(0) (0.002 g). The suspension was filtered through Celite and the solvent evaporated at reduced pressure. The residue was chromatographed over silics gel, eluting with ethyl acetate/hexane mixtures to provide the title compound as a white foam (0.213 g); ν_{max} (CH_2Cl_2) 3383, 1784, 1755, 1735, 1686 cm^{-1}.

Step 3. Mutilin 14-[*N*-(*N*-*t*-butoxycarbonyl- nipecotyl)carbamate]

The product from Step 2 was dissolved in tetrahydrofuran (2 ml) and stirred vigorously at room temperature for 1.5 h with 1M sodium hydroxide solution (0.407 ml). The reaction solution was diluted with ethyl acetate, washed with brine, dried ($MgSO_4$) and evaporated. Silica gel column chromatography provided the title compound as a diastereoisomeric mixture and an oil (0.103 g); ν_{max} (CH_2Cl_2) 3540, 3419, 1783, 1732, 1697 cm^{-1}; MS (ES) *m/z* 573 ($[M-H]^-$).

Step 4. Mutilin 14-[*N*-(nipecotyl)carbamate]

The product from Step 3 (0.08 g) was dissolved in dichloromethane (2 ml) and stirred at room temperature for 16 h with trifluoracetic acid (0.120 ml). The solvent was then evaporated and the residue was partitioned between ethyl acetate and saturated sodium hydrogen carbonate solution. The organic solution was washed with brine, dried ($MgSO_4$) and evaporated at reduced pressure. Silica gel column chromatography, eluting with a gradient of 0-10% methanol/35% ammonia solution (9:1) in dichloromethane provided the title compound as a diastereoisomeric mixture and as a white foam (0.035 g); ν_{max} (CH_2Cl_2) 1771, 1734, 1702cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 0.78 (3H, 2 x d, 6.9 Hz), 0.89 (3H, d, 7.02), 1.20 (3H, 2 x s,), 1.48 (3H, s), 3.32-3.41 (1H, broad res.), 5.22 (1H, d, J17.3Hz), 5.37 (1H, d, J11.1Hz), and 6.60 (1H, 2 x dd, J10.9, 17.3Hz); MS (CI) *m/z* 475 (MH^+).

Example 166. Mutilin 14-[*N*-(4-amino-3-methoxybenzoyl)]-carbamate

Step 1. 3-Methoxy-4-Nitrobenzoyl chloride

To a stirred solution of 3-methoxy-4-nitrobenzoic acid (1.21g, 6.24mmol) in dry dichloro- methane (6ml) was added oxalyl chloride (1.1ml) followed by *N,N*-dimethylformamide (1 drop). The mixture was stirred at room temperature under argon for 3 hours. The solvent was evaporated *in vacuo*. The residue was purified by chromatography on silica gel eluting with 50% ethyl acetate in hexane to yield the title compound (0.89g, 66%); ν_{max} (CH_2Cl_2) 1771cm^{-1}; MS (EI) *m/z* 215 (M^+). Found M^+ 214.9984, $C_8H_6NO_4Cl$ requires 214.9985.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin-14-[*N*-(3-methoxy-4-nitrobenzoyl)]-carbamate

Silver cyanate (669mg, 4.5mmol) was suspended in dry dichloromethane (10ml) under an atmosphere of argon. A solution of the acid chloride from Step 1 (0.89g, 4.1mmol) in dichloromethane (10ml) was added and the heterogeneous mixture stirred at reflux under subdued light. After 40 minutes the reaction was allowed to cool and treated with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (668mg, 2.0mmol) and the reaction stirred for 17 hours. The mixture was filtered through celite. The extract was washed with saturated sodium hydrogen carbonate (x2) and brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. The residue was purified by chromatography on silica gel eluting with 20, 30 and 40% ethyl acetate in hexane to yield the title compound (720mg, 65%) ν_{max} (CH_2Cl_2) 3054, 2987, 1780, 1698 and 1421cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 3.23 (3H,s), 3.42-3.52 (1H,m), 4.03 (3H, s), 5.03 (1H, d, *J* 17.4Hz), 5.31 (1H, d, *J* 10.7Hz), 5.86 (1H, d, *J* 9.9Hz), 6.66 (1H, dd, *J* 10.7, 17.5Hz), 7.34 (1H, dd, *J* 1.6, 8.3Hz), 7.62 (1H, d, *J*, 1.6Hz), 7.89 (1H, d, *J* 8.3Hz), 8.07 (1H, bs); MS (CI) *m/z* 574.3 (MNH_4^+).

Step 3. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin-14-[*N*-(4-amino-3-methoxybenzoyl)]-carbamate

(3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N* (3-methoxy-4-nitro- benzoyl)] carbamate (720mg, 1.29mmol) was suspended in ethanol (30ml). Addition of ethyl acetate (6ml) with warming brought about complete dissolution. Tin(II) chloride (1.26g, 6.65mmol) was added and the reaction warmed to reflux whilst under an atmosphere of argon. After 4 hours the solvent was evaporated *in vacuo* and the residue taken up in ethyl acetate and water, an emulsion was

formed and removed by filtration through Kieselguhr. The organic phase was neutralised with sodium hydrogen carbonate (x2), washed with brine and dried ($MgSO_4$). The residue was purified by chromatography on silica gel eluting with 20, 30, 40 and 60% ethyl acetate in hexane to yield the title compound (211mg, 31%); ν_{max} (CH_2Cl_2) 3100, 2986, 1771, 1698, 1617 and 1479cm^{-1}; ^{1}HNMR ($CDCl_3$) *inter alia* 3.22 (3H, s), 3.42-3.50 (1H, m), 3.91 (3H, s), 4.32 (2H, s), 5.01 (1H, d, *J* 17.5Hz), 5.29 (1H, d, *J* 10.7Hz), 6.66 (1H, d, *J* 8.2Hz), 6.75 (1H, dd, *J* 10.6, 17.5Hz), 7.20 (1H, dd, *J* 1.9, 8.2Hz),7.40 (1H,d, *J* 1.8Hz), 7.99 (1H,bs); MS (EI) *m/z* 526 (M^+).

Step 4. Mutilin-14-[*N*-(4-amino-3-methoxybenzoyl)]-carbamate

The product of Step 3 (191mg, 0.36mmol) in dioxan (2ml) was treated with a saturated solution of zinc chloride in conc. HCl (2ml) and the reaction stirred at room temperature for 1 hour. The solution was poured into ethyl acetate and saturated sodium hydrogen carbonate solution. The aqueous phase was re-extracted with ethyl acetate (x2) and the combined organic phases were washed with brine. The organic phase was dried ($MgSO_4$) and the solvent evaporated *in vacuo*. The residue was purified by chromatography on silica gel eluting with 60, 70, 80, 90 and 100% ethyl acetate in hexane to yield the title compound 56mg, 30%); ν_{max} (CH_2Cl_2) 3100, 2986, 1772, 1733, 1617 and 1479cm^{-1}; ^{1}H NMR ($CDCl_2$), *inter alia* 3.34-3.41 (1H, m), 3.90 (3H, s), 4.29 (2H, s), 5.27 (1H, dd, *J* 1.4, 17.4Hz), 5.36 (1H, dd, *J*1.4, 11.0Hz), 5.83 (1H, d, *J* 8.4Hz), 6.58 (2H, dd, *J* 8.9, 15.3Hz), 6.65 (1H, d, *J* 6.2Hz), 7.17 (1H, dd, *J* 1.9 ,8.2Hz), 7.37 (1H, d, *J* 1.8Hz),7.85 (1H,bs); MS (NH_3DCI) *m/z* 513 (MH^+).

Example 167. Mutilin-14-[*N*-(4-fluorobenzoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin-14-[N-(4-fluorobenzoyl)]-carbamate

4-Fluorobenzoyl chloride (0.57ml, 4.82mmol) was reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (978mg, 2.92mmol) and silver cyanate (787mg, 5.25mmol) in dichloromethane (12ml), as for Example 166, Step 2, to afford the title compound (979mg, 82%); ν_{max} (CH_2Cl_2) 3420, 3054, 2986, 1778, 1698, 1604 and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 3.23 (3H, s), 3.42-3.50 (1H, m), 5.02 (1H, d, *J* 17.5Hz), 5.28 (1H, d, *J* 9.9Hz), 5.85 (1H, d, *J* 10.0Hz), 6.70 (1H, dd, *J* 10.7 ,17.5Hz), 7.14-7.21 (2H, m), 7.84-7.89 (2H, m),8.07 (1H,bs); MS (CI) *m/z* 517 (MNH_4^+).

Step 2. Mutilin 14-[*N*-(4-fluorobenzoyl)]-carbamate

The product of Step 1 (959mg, 1.92mmol) in dioxane (12ml) was treated with a saturated solution of zinc chloride in conc. HCl (12ml), as for Example 166, Step 4, to afford the title compound (140mg, 15%); ν_{max} (CH_2Cl_2) 3414, 3054, 2987, 1779, 1684, 1604, and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 3.33-3.40 (1H, m), 5.22 (1H, dd, *J* 1.4 ,17.4Hz), 5.33 (1H, dd, *J* 1.4, 10.9Hz), 5.81 (1H, d, *J* 8.5Hz), 6.52 (1H, dd, *J* 11.0, 17.3Hz), 7.03-7.17 (2H, m), 7.80-7.88 (2H, m), 8.30 (1H, bs); MS (Electrospray) *m/z* 503 (MNH_4^+).

Example 168. Mutilin 14-[*N*-(4-methylsulphonyl benzoyl)]-carbamate

Step 1. 4-Methylsulphonylbenzoyl chloride

To a stirred solution of 4-methylsulphonyl benzoic acid (1g, 4.99mmol) in dry dichloromethane (10ml) was added oxalyl chloride (0.88ml, 9.87mmol) followed by *N,N*- dimethyl formamide (2 drops). The reaction was stirred at room temperature under argon for 5 hours. The solvent was evaporated *in vacuo*. The product was used immediately in the next reaction; ν_{max} (CH_2Cl_2) 1784cm^{-1}.

Step 2. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-methyl- sulphonyl benzoyl]-carbamate

The product from Step 1 in dichloromethane (12ml) was treated with silver cyanate (787mg, 5.25mmol) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (814mg, 2.43mmol) and the reaction stirred for 2 hours. The title compound was isolated by the same procedure as described in Example 166, Step 2, (1.19g, 91%); ν_{max} (CH_2Cl_2) 3064, 2984, 1780, 1718 and 1476cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 3.09 (3H, s), 3.23 (3H, s), 3.42-3.49 (1H, m), 5.03 (1H, d, *J* 17.4Hz), 5.31 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 9.9Hz), 6.68 (1H, dd, *J* 10.7 ,17.5Hz), 7.96-8.00 (2H, m), 8.04-8.07 (2H, m), 8.12 (1H, bs); MS (Electrospray) *m/z* 558 ($M-H^-$).

Step 3. Mutilin 14-[*N*-(4-methylsulphonyl benzoyl)]-carbamate

The product of Step 2 (1.17g, 2.14mmol) in dioxane (13ml) was treated with a saturated solution of zinc chloride in conc. HCl (13ml), as for Example 166, Step 4, to afford the title compound (342mg, 30%); ν_{max} (CH_2Cl_2) 3057, 2936, 1782, 1733 and 1478cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 3.08 (3H, s), 3.38 (1H, dd, *J* 10.7, 6.6Hz), 5.2H (1H, dd, *J* 17.4, 1.4Hz), 5.38 (1H, dd, *J* 10.9, 1.3Hz), 5.82

(1H, d, *J* 8.5Hz), 6.53 (1H, dd, *J* 11.1 ,17.4Hz), 7.94-7.97 (2H, m), 8.02-8.05 (2H, m), 8.07 (1H, s); MS (Electrospray) *m/z* 544 ($M-H^-$).

Example 169. Mutilin 14-[*N*-(3-(2-Dimethylaminoethoxy)-4-fluorobenzoyl)]-carbamate

Step 1. 4-Fluoro-3-hydroxybenzoic acid

Sulphuric acid (concentrated, 11ml) was stirred and heated to 90°C. 2-Fluoro-5-trifluoro- methylphenol (2.5g, 13.88mmol) was added portion wise during 25 minutes. The mixture was heated to 120°C for 10 minutes. The mixture was cooled to ambient temperature and poured onto a mixture of ice and water. The precipitate was isolated, washed with water and dried, to afford the title compound (1.01g, 47%); ν_{max} (CH_2Cl_2) 3420, 3054, 2987, 1636 and 1422cm^{-1}; MS (EI) *m/z* 156 (M^+). Found M^+ 156.0223, $C_7H_5O_3F$ requires 156.0223.

Step 2. 3-Acetoxy-4-fluorobenzoic acid

The product from Step 1 (1.0g, 6.41mmol) in dichloromethane (35ml) was treated with triethylamine (1.95ml, 12.97mmol) and 4-dimethylaminopyridine (24.7mg, 0.20mmol). The reaction was cooled in an ice-bath and treated with acetic anhydride (0.62ml, 6.57mmol) and stirred for 2 hours at room temperature under argon. The solution was washed with HCl (5M) and water, dried ($MgSO_4$) and the solvent evaporated *in vacuo* to afford the title compound (1.08g, 86%); ν_{max} (CH_2Cl_2) 3054, 2987, 1777, 1670 and 1422cm^{-1}; MS (Electrospray) *m/z* 197 ($M-H^-$). Found M^+ 198.0326, $C_9H_7O_4F$ requires 198.0328.

Step 3. 3-Acetoxy-4-fluorobenzoyl chloride

The product from Step 2 (1.06g, 5.35mmol) in dichloromethane (14ml) was treated with oxalyl chloride (0.60ml, 6.88mmol) followed by *N,N*-dimethylformamide (1 drop), as for Example 168, Step 1. The product was used immediately in the next reaction ν_{max} (CH_2Cl_2) 1778cm^{-1}.

Step 4. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(3-acetoxy-4- fluorobenzoyl]-carbamate

The product from Step 3 in dichloromethane (20ml) was treated with silver cyanate (0.84g, 5.60mmol) and (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (0.64g, 1.92mmol) and the reaction stirred for 3 hours. The title compound (70% pure) was isolated by the same procedure as described in

Example 166, Step 2, (1.06g, 96%); ν_{max} (CH_2Cl_2) 3418, 3054, 2986, 1779, 1697 and 1422cm^{-1}; MS (Electrospray) *m/z* 556 ($M-H^+$).

Step 5. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-fluoro- 3-hydroxybenzoyl]-carbamate

The product from Step 4 (1.06g, 1.90mmol of 70% pure material) in dioxane (15ml) was treated with 1.0M sodium hydroxide solution (7ml) for 3 hours at room temperature. The reaction was poured into ethyl acetate and dilute HCl. The aqueous phase was re-extracted with ethyl acetate. The organic phase was washed with brine, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residue was purified by chromatography on silica gel eluting with 20, 30, 40 and 50% ethyl acetate in hexane to afford the title compound (420mg, 43%); ν_{max} (CH_2Cl_2) 3420, 3054, 2986, 1778, 1697, and 1480cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 2.52 (1H, dd, *J* 10.1, 15.3Hz), 2.90 (1H, q, *J* 6.3Hz), 3.23 (1H, s), 3.42-3.49 (1H, m), 5.01 (1H, d, *J* 17.5Hz), 5.27 (1H, d, *J* 10.7Hz), 5.85 (1H, d, *J* 9.9Hz), 6.69 (1H, dd, *J* 10.7 and 17.5Hz), 7.14-7.21 (1H, m), 7.33-7.39 (1H, m), 7.52-7.56 (1H, m), 8.05 (1H, bs); MS (ES) *m/z* 516 (MH^+). Found 515.2686 $C_{29}H_{38}NO_6F$ requires 515.2683.

Step 6. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-*N*-[3-(2-dimethyl- aminoethoxy)-4-fluorobenzoyl]-carbamate

The product from Step 5 (400mg, 0.78mmol) was dissolved in acetone (6ml) and treated with dimethylaminoethylchloride hydrochloride (113mg, 0.78mmol) and potassium carbonate (213 mg). The reaction was heated to reflux for 12 hours under argon. The reaction was diluted with ethyl acetate and washed with brine and water. The organic phase was dried ($MgSO_4$) and the solvent removed *in vacuo*. The residue was purifed by chromatography on silica gel eluting with 25 and 50% ethanol in ethyl acetate to afford the title compound (150mg, 33%); ν_{max} (CH_2Cl_2) 3054, 2986, 1777, 1698 and 1480cm-1; ^{1}H NMR ($CDCl_3$) 2.38 (6H, s), 2.55 (1H, dd, *J* 10.1, 15.2Hz), 2.81 (2H, t, *J* 5.7Hz), 2.91 (1H, dd, *J* 6.5, 12.9Hz), 3.23 (3H, s), 3.43-3.50 (1H, m), 4.21 (2H, t, *J* 5.7Hz), 5.03 (1H, d, *J* 17.4Hz), 5.31 (1H, d, *J* 10.7Hz), 6.72 (1H, dd, *J* 10.7 and 17.5Hz), 7.12-7.20 (1H, m), 8.02 (1H, bs).

Step 7. Mutilin 14-*N*-[3-(2-dimethylaminoethoxy)-4-fluorobenzoyl]-carbamate

The product from Step 6 (80mg, 0.14mmol) in dioxane (1ml) was treated with conc. HCl (1ml) and the reaction stirred at room temperature for 4 hours. The

title compound was isolated by the same procedure as described in Example 166, Step 4, (65mg, 76%); ν_{max}.(CH_2Cl_2) 3054, 2988, 1777, 1732, 1609 and 1422cm^{-1}. ^{1}H NMR ($CDCl_3$) *inter alia* 2.45 (6H, s), 2.91 (2H, t, *J* 5.5Hz) 3.37 (1H, d, *J* 6.4Hz), 4.28 (2H, t, *J* 5.5Hz), 5.23 (1H, dd, *J* 1.3, 17.4Hz), 5.36 (1H, dd, *J* 1.3, 11.1Hz), 5.83 (1H, d, *J* 8.4Hz), 6.55 (1H, dd, *J* 11.0, 17.3Hz), 7.10-7.19 (1H, m), 7.33-7.39 (1H, m), 7.55-7.62 (1H, m), 8.33 (1H, bs); MS (ES) *m/z* 573 ($M+H^+$), 571 ($M-H^-$).

Example 170. Mutilin 14-{*N*-[4-(2-dimethylaminoethyloxy)-benzoyl]}-carbamate hydrochloride

Step 1 (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-{*N*-[4-(2-dimethyl- aminoethyloxy)benzoyl]}-carbamate

A solution of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(4-hydroxy- benzoyl)]-carbamate (1g, 2mmole) in acetone (20ml) was treated with powdered K_2CO_3 (560mg) and 2-dimethylaminoethylchloride hydrochloride (290mg), and stirred at reflux under argon for 11 hours. The mixture was diluted with EtOAc, washed with water, dried and evaporated. Chromatography on silica, eluting with 2:1 EtOAc/ EtOH gave the title compound as a yellow foam (0.51g, 45%); ν_{max} ($CHCl_3$) 3436, 1775, 1697, 1606, 1579, 1512, 1488, 1168cm^{-1}; ^{1}H NMR δ ($CDCl_3$) 0.87 (3H, d, *J* 6.7Hz), 0.98 (3H, d, *J* 6.3Hz), 1.0-1.6 (12H, m), 1.6-1.75 (2H, m), 1.85-2.05 (2H, m), 2.1-2.2 (1H, m), 2.32 (6H, s), 2.4-2.55 (1H, m), 2.73 (2H, t, *J* 5.5Hz), 2.87 (1H, q, *J* 6.3Hz), 3.18 (3H, s), 3.35-3.5 (1H, m), 4.08 (2H, t, *J* 5.5Hz), 4.95 (1H, d, *J* 17.5Hz), 5.22 (1H, d, *J* 10.7Hz), 5.81 (1H, d, *J* 9.8Hz), 6.67 (1H, dd, *J* 17.5 and 10.7Hz), 6.94 (2H, d, *J* 8.8Hz), 7.81 (2H, d, *J* 8.8Hz); MS (ammonia CI) *m/z* 569 (MH^+, 10%), 352 (20%), 317 (70%), 303 (50%), 235 (100%), 209 (70%); (negative ion electrosprany) *m/z* 567 ($M-H^-$, 100%).

Step 2 Mutilin 14-{*N*-[4-(2-dimethylaminoethyloxy)-benzoyl]}-carbamate

The product from Step 1 (0.5g) in dioxan (6ml) was ice-cooled, treated with a saturated solution of $ZnCl_2$ in conc. HCl (2ml) and stirred at room temp. for 5 hours. The mixture was diluted with EtOAc, washed with excess aqueous $NaHCO_3$ and water, dried and evaporated. Chromatography on silica, eluting with 3:1 and then 1:1 EtOAc/EtOH, gave the title compound as a gum (230mg, 47%); ν_{max} ($CHCl_3$) 3565, 3442, 1777, 1731, 1709, 1606, 1579, 1513, 1469cm^{-1}; ^{1}H NMR δ($CDCl_3$) 0.79 (3H, d, *J* 6.4Hz), 0.87 (3H, d, *J* 6.9Hz), 1.0-1.2 (4H, m), 1.3-1.8 (11H, m), 2.0-2.3 (5H, m), 2.36 (6H, s), 2.78 (2H, t, *J* 5.5Hz), 3.36

(1H, d, *J* 6.3Hz), 4.11 (2H, t, *J* 5.5Hz), 5.20 (1H, dd, *J* 17.5 and 1.3 Hz), 5.31 (1H, dd, *J* 11 and 1.1 Hz), 5.80 (1H, d, *J* 8.3Hz), 6.52 (1H, dd, *J* 17.5 and 11Hz), 6.95 (2H, d, *J* 8.9Hz), 7.79 (2H, d, *J* 8.9Hz), 8.40 (1H, s); MS (EI) *m/z* 554 (M^+, 5%), 163 (100%); (NH_3DCI) *m/z* 555 (MH^+, 30%), 235 (100%).

Step 3 Mutilin 14-{*N*-[4-(2-dimethylaminoethyloxy)benzoyl]}-carbamate hydrochloride

The product from Step 2 (225mg) in EtOAc (5ml) was treated with 4M HCl in dioxan (0.25ml). The solvents were evaporated to leave the product as a white solid (193mg). ν_{max} ($CHCl_3$) 3676, 3434, 2287 (br), 1778, 1733, 1654, 1607, 1468cm^{-1}; ^1H NMR δ($(CD_3)_2SO$) 0.70 (3H, d, *J* 5.9Hz), 0.83 (3H, d, *J* 7.7Hz), 1.0-1.2 (4H:, m), 1.2-1.8 (10H, m), 2.0-2.3 (4H, m), 2.42 (1H, s), 2.83 (6H, s), 3.4-3.6 (3H, m), 4.43 (2H, t, *J* 5Hz), 4.55 (1H, d, *J* 5.9Hz, disappears on D_2O exchange), 5.0-5.2 (2H, m), 5.60 (1H, d, *J* 7.8Hz), 6.26 (1H, dd, *J* 17.5 and 11.1Hz), 7.10 (2H, d, *J* 8.9Hz), 7.88 (2H, d, *J* 8.9Hz), 10.36 (1H, br s, disappears on D_2O exchange), 10.63 (1H, s, disappears on D_2O exchange).

Example 171. Mutilin 14-{N-[4-(glucosyloxy)-benzoyl]}-carbamate

Step 1. Mutilin 14-{N-[4-(tetra-O-acetyl-glucosyloxy)-benzoyl]}-carbamate

A solution of acetobromo-alpha-D-glucose (411mg, 1 mmol) in acetone (2 ml) was added to a solution of mutilin 14-[N-(4-hydroxy-benzoyl)]-carbamate(483 mg, 1 mmol) and 1N sodium hydroxide (1ml) in water (2 ml) and acetone (5 ml). After three hours at room temeperature a further portion of 1N sodium hydroxide (1 ml) was added followed by acetobromo-alpha-D-glucose (411 mg) in acetone (2 ml). The mixture was left overnight at room temperature and then diluted with water and extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$) and evaporated to a foam which was chromatographed on silica gel, using 20% acetone-toluene to give the product as a white foam (140 mg): Rf 0.2; ν_{max} ($CHCl_3$) 3439 w, 1757 br, 1721 (shoulder) cm-1.; ^1H NMR (d_6 acetone) *inter alia* 8.6 (1H, br s, NH), 7.80-7.82 (2H, arom), 7.02-7.04 (2H, arom), 6.57 (1H, dd, J 17.5, 11), 5.81 (1H, d, J 8, H-14), 5.35 (1H, dd, J 11, 1.5), 5.32 (1H, dd, J 9, 9, gluc H-3), 5.28 (1H, dd, J 9,9, gluc H-2), 5.23 (1H, dd, J 17.5, 1.5), 5.21 (1H, d, J 7.4, gluc H-1), 5.16 (1H, dd, J 9,9, gluc H-4), 4.28 (1H, dd J12.3, 5.5, gluc H-6), 4.17 (1H, dd, J12.3, 2.5, gluc H-6), 3.94 (1H, ddd, J 7.9, 5.5, 2.5, gluc H-5), 3.40 (1H, dd, J 10.4, 6.5); ^{13}C NMR *inter alia* 169.2, 169.4, 170.1 and 170.4 (4x C=O of acetate), 98.2 (CH of glucoside); MS (+ve ion electrospray) *m/z* 814 (MH^+), 831 (MNH_4^+), 836 (MNa^+).

Step 2. Mutilin 14-{N-[4-(glucosyloxy)-benzoyl]}-carbamate

The product of Step 1 (117 mg, 0.14 mmol) was partly dissolved in methanol (4 ml) and triethylamine (0.02 ml) was added. The mixture was stirred at room temperature for a total of 48h during which time further portions of triethyalmine (0.02 ml x 2) were added while monitoring the reaction by tlc. The mixture was evaporated to dryness and chromatographed on silica gel, using 20% methanol-chloroform giving the title compound as a white solid (55 mg, 61%): Rf 0.33; ^{1}H NMR (d_6 acetone) *inter alia* 8.00(1H, br s, NH), ca7.9 (2H, arom), ca7.15 (2H, arom), 6.46 (1H, dd, J 17.6, 11), 5.77 (1H, d, J 8, H-14), 5.25 (1H, dd, J 17.6, 2), 5.18 (1H, dd, J 11, 2), 4.60 (1H, d J 3.5, exch D_2O), 4.35 (1H, d, J 3.5, exch D_2O), 4.27 (1H, d, J3.5 exch D_2O), 3.87 (1H, dd, J 11.8, 1.4 with D_2O); MS (-ve ion electrospray) *m/z* 644 (100%, M-H$^-$).

Example 172. Mutilin 14-[N-(2-azido-phenyl-acetyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[N-(2-azido-phenyl-acetyl)]-carbamate

A solution of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (667 mg, 2 mmol) in dichloromethane (25 ml) was added to a stirred mixture of D(-)-alpha-azido-phenylacetyl chloride (5mmol) and siver cyanate (750 mgs, 5 mmol) in dichloromethane (10 ml). The mixture was stirred overnight at room temperature, filtered and evaporated to dryness. The crude product was chromatographed on silica gel, eluting with 5% acetone-toluene to give the title compound as a white solid (841 mg, 80%), Rf 0.32; ν_{max} ($CHCl_3$) 3389, 2119, 1787, 1756, 1719, 1697 cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 8.0 (1H, br s, exch D_2O), 7.42 (5H, arom), 6.49 (1H, dd, J ca 18, 10.7), 5.70 (1H, d, J 10), 5.52 (1H, brs, PhC*H*-CO), 5.26 (1H, d, J 10.7); MS (-ve ion electrospray) *m/z* 535 (M-H$^-$).

Step 2. Mutilin 14-[N-(2-azido-phenyl-acetyl)]-carbamate

The product of Step 1 (536 mg, 1 mmol) was dissolved in dioxan (15 ml) and a saturated solution of zinc chloride in conc hydrochloric acid (4 ml) was added with cooling in bath of cold water. The clear yellow solution was stirred at room temperature for 3.5 hour. The mixture was diluted with cold aq. sodium bicarbonate and extracted with ethyl acetate. The extract was washed with water and with brine and dried ($MgSO_4$). Evaporation gave a crude product which was purified by chromatography on silica gel eluting with 5% acetone-toluene giving the title compound as a white foam (413 mg, 79%); Rf 0.05; ν_{max} ($CHCl_3$)

3565, 3388, 2112, 1789, 1756 (shoulder), 1725 cm^{-1} ; ^1H NMR ($CDCl_3$) *inter alia* 7.84 (1H, br s), 7.40 (5H, arom), 6.38 (1H, dd, J 17, 11), 5.67 (1H, d, J 8.5), 5.54 (1H, br s, PhC*H*-CO), 5.23 (1H, d, J 11), 5.11 (1H, d, J 17); 3.33 (1H, dd, J 10.5, 6.5); MS (+ve ion electrospray) *m/z* 540 (MNH_4^+), MS (-ve ion electrospray) *m/z* 521 (100%, $M-H^-$).

Example 173. 19,20-Dihydro-mutilin 14-[N-(alpha-amino-phenylacetyl)]-carbamate hydrochloride

Mutilin 14-[N-(2-azido-phenyl-acetyl)]-carbamate (240 mg, 0.46 mmol) (Example 172) was dissolved in dioxan (5 ml) and water (1 ml) and 4M HCl in dioxan (0.25 ml) was added. The solution was shaken with 10%Pd-C (100mg) in an atmosphere of hydrogen for 45 minutes. The catalyst was removed by filtration and washed with aqueous dioxan. The filtrate was evaporated to an oil and azeotroped with ethanol and with chloroform. The resulting crude solid was recrystallised from ethanol-ether to give the title compound as an off-white solid (123 mg, 50%), mp 175-180 °C; ν_{max} ($CHCl_3$) ca 2600-3200, 1757, 1733, 1703 cm^{-1} ; ^1H NMR (d_4 methanol) *inter alia* 7.49 (5H, arom), 5.72 (1H, br, PhC*H*-CO), 5.55 (1H, d, J 8), 3.41(1H, d, J 6); ^{13}C NMR ($CDCl_3$- d_4 methanol) *inter alia* 7.7, 10.9, 14.5, 16.0, 20.4, 24.7, 26.0, 26.7, 30.2, 34.4 (CH and CH_2), 36.5, 40.5, 40.7, 41.9, 45.5, 57.0, 58.4, 71.5, 75.9, 128.5, 129.2, 130.0, 131.4, 150.5, 169, 218.0; MS (NH_3 DCI) *m/z* 499 (100%, MH^+); MS(glycerol FAB) Found *m/z* 499.3170 (MH^+) $C_{29}H_{43}N_2O_5$ requires 499.3172.

Example 174. Mutilin 14-[N-(cyclohexyl-acetyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[N-(cyclohexyl-acetyl)]-carbamate

A solution cyclohexyl-acetyl isocyanate (2.5 mmol) in dichloromethane (10 ml) was added to one of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (334 mg, 1 mmol) in dichloromethane (3 ml) at room temerature. The solution was stirred ovemight at room temperature and evaporated to dryness. The crude product was chromatographed on silica gel, eluting with ethyl acetate 1:2 to give the title compound as a white foam (252 mg, 50%), Rf 0.42; ν_{max} ($CHCl_3$) 3395, 1782w, 1749, 1697 cm^{-1}.; ^1H NMR ($CDCl_3$) *inter alia* 7.47 (1H, br s, exch D_2O), 6.64 (1H, dd, J 17.5, 10.5), 5.74 (1H, d, J 10), 5.33 (1H, d, J 10.5), 5.03 (1H, d, J 17.5), 3.4-3.5 (1H, m); MS (NH3 DCI)) *m/z* 519 (8%, MNH_4^+).

Step 2. Mutilin 14-[N-(cyclohexyl-acetyl)]-carbamate

The product of Step 1 (400 mg, 0.8 mmol) was dissolved in dioxan (4 ml) and a saturated solution of zinc chloride in conc hydrochloric acid (2 ml) was added. The solution was stirred at room temperature for 2 hour and then diluted with cold aq. sodium bicarbonate and extracted with ethyl acetate. The extract was washed with aq. sodium bicarbonate and with brine and dried ($MgSO_4$). Evaporation gave a crude product which was purified by chromatography on silica gel eluting with ethyl acetate 1:2 giving the title compound as a white solid (152 mg, 39%); mp 198-200 °C; ν_{max} ($CHCl_3$) 3397, 2928, 1735, 1712 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 7.29 (1H, br s), 6.49 (1H, dd, J 17.3, 11), 5.70 (1H, d, J 7.5), 5.38 (1H, dd, J 11, 1.4), 5.23 (1H, d, J 17.3, 1.4); 3.36 (1H, dd, J 10.5, 6.5), 2.62 (2H, d, J6.6); MS (-ve ion electrospray) *m/z* 486 (50%, $M-H^-$).

Example 175. Mutilin 14-[N-(cinnamoyl)]-carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[N-(cinnamoyl)]-carbamate

A solution cinnamoyl isocyanate (2 mmol) in dichloromethane (5 ml) was added to one of (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (501 mg, 1.5 mmol) in dichloromethane (5 ml) at room temerature. The solution was stirred for 1 hour and a further portion of cinnamoyl isocyanate (1 mmol) in dichloromethane (2.5 ml) was added. The mixture was stirred at room temperature for 2 days and evaporated to dryness. The crude product was chromatographed on silica gel, eluting with ethyl acaetate 1:4 to give the title compound as a white solid (710 mg, 93%), Rf 0.38; ν_{max} ($CHCl_3$) 3400, 1776w, 1747, 1690, 1621 cm^{-1}.; ^1H NMR ($CDCl_3$) *inter alia* 7.89 (1H, d, J 16), 7.59-7.65 (2H, m), 7.58 (1H, d, J 16), 7.50 (1H, br s, exch D_2O), 7.4-7.5 (3H, m), 6.68 (1H, dd, J 17.5, 10.5), 5.78 (1H, d, J 10), 5.36 (1H, d, J 10.5), 5.05 (1H, d, J 17.5), 3.4-3.5 (1H, m), 3.23 (3H, s); MS (NH_3 DCI)) *m/z* 508 (MH^+), 525 (MNH_4^+).

Step 2. Mutilin 14-[N-(cinnamoyl)]-carbamate

The product of Step 1 (507 mg, 1 mmol) was dissolved in dioxan (4 ml) and a saturated solution of zinc chloride in conc hydrochloric acid (2 ml) was added. The solution was stirred at room temperature overnight and then diluted with cold aq. sodium bicarbonate and extracted with ethyl acetate. The extract was washed with water and with brine and dried ($MgSO_4$). Evaporation gave a crude

product which was purified by chromatography on silica gel eluting with ethyl acetate 1:2 giving the title compound as a white solid (316 mg, 64%); mp 148-151 °C; ν_{max} ($CHCl_3$) 3400, 1735, 1682, 1622 cm^{-1}; MS (NH_3 DCI)) *m/z* 494 (10%, MH^+), 511 (12%, MNH_4^+).

Example 176. 19,20-Dihydro-mutilin 14-(1-Methylpiperidin-4-oyl)-carbamate

Mutilin 14-(1-methylpiperidin-4-oyl)-carbamate (100mg) as a solution in THF (5ml) with 10% palladium/carbon catalyst was hydrogenated for 1 hour at room temperature. The catalyst was filtered off through celite and the solution concentrated to give the title compound as a colourless solid, (100mg, quant.); ν_{max} (CH_2Cl_2) 3630(w), 3390(w), 1732, 1710 1470 and 1406 cm^{-1}; ^1H NMR ($CDCl_3$) *inter alia* 1.40 (3H, s), 1.43 (3H, s), 2.89 (2H, d *J* 11.4Hz), 3.07 (1H, m), 3.41 (1H, d, *J* 6.0Hz), 5.55 (1H, d, *J* 8.03Hz) and 7.38 (1H, s); MS(EI) m/z 490 (M^+) (Found: M^+, 490.341; $C_{28}H_{46}N_2O_5$ requires 490.341).

Example 177. 19,20-Dihydro-mutilin 14-(1-Methylpiperidin-4-oyl)-carbamate hydrochloride

19,20-Dihydro-mutilin 14-(1-methylpiperidin-4-oyl)-carbamate (348mg) in ethyl acetate at room temperature was vigorously stirred and treated with 1M hydrochloric acid in ether in a dropwise fashion until no further precipitation was observed. The title compound was filtered off and dried *in vacuo* over 12 hours, and was thus obtained as a white solid (302mg, 81%); ^1H NMR (D_2O) *inter alia* 0.68 (6H, m), 0.86 (3H, d, *J* 7.2Hz), 2.85 (3H,s), 3.04 (2H, d, *J* 11.0), 3.55 (3H, m) and 5.56 (1H, d *J* 7.8Hz).

Example 178. 19,20-Dihydromutilin 14-{*N*-[(3*S*,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl]}-carbamate

A solution of mutilin 14-{*N*-[(3*S*,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl]}-carbamate (95 mg, 0.20 mmol) in 1:1 ethanol:tetrahydrofuran (10ml) was hydrogenated for 12 hours over 10% palladium on carbon (90mg). The solution was filtered through celite and the solvent evaporated *in vacuo* to yield the title compound (85 mg, 87%); ν_{max} (KBr) 3421, 2957, 1772, 1733, 1702 and 1464cm^{-1}; ^1H NMR (d_6-DMSO) *inter alia* 0.68 (3H, d, *J* 7.1Hz), 0.82 (3H, d, *J* 6.8Hz), 4.46 (1H, d, *J* 5.9Hz), 5.46 (1H, d, *J* 7.6Hz), 10 53 (1H, bs); MS (EI) *m/z* 488 (M^+). Found: M^+, 488.3256; $C_{28}H_{44}N_2O_5$ requires 488.3250.

Example 179. 19,20-Dihydromutilin 14-[*N*-(quinuclidine-4-carbonyl)]-carbamate

A solution of mutilin 14-[*N*-(quinuclidine-4-carbonyl)]-carbamate (100 mg, 0.20 mmol) in 2:1 tetrahydrofuran:ethanol (30ml) was hydrogenated for 1 hour over 10% palladium on carbon (10mg). The solution was filtered through celite and the solvent evaporated *in vacuo* to yield the title compound as a white solid (90 mg, 90%); $\nu_{max}(CH_2Cl_2)$ 2960, 1782, 1733, 1716 and 1479cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 0.69 (3H, d, *J* 6.6Hz), 3.42 (1H, d, *J* 5.9Hz), 5.61 (1H, d, *J* 8.2Hz), 7.37 (1H, bs); MS (EI) *m/z* 502 (M^+). Found: M^+, 502.3411; $C_{29}H_{46}N_2O_5$ requires 502.3407.

Example 180. 19,20-Dihydro-mutilin 14-[*N*-(3-(2-Dimethylaminoethoxy)-4-fluorobenzoyl)]-carbamate

Mutilin 14-[*N*-(3-(2-dimethylaminoethoxy)-4-fluorobenzoyl)]-carbamate (0.200 g) was dissolved in ethanol (30 ml) and shaken at ambient temperature and atmospheric pressure with hydrogen in the presence of 10% palladium on charcoal catalyst for 2 hours. The supension was filtered through Celite and the filtrate evaporated to yield the title compound as a white foam (0.201 g); ^{1}H NMR *inter alia* ($CDCl_3$) 0.75 - 0.85 (6H, m), 0.90 - 1.05 (6H, m), 1.51 (3H, s), 2.38 (6H, s), 2.79 (2H, t, J 5.61 Hz), 3.41 (1H, d, J 5.95 Hz), 4.20 (2H, t, J 5.64 Hz), 5.70 (1H, d, J 8.03 Hz), 7.11 (1H, dd, J 8.43 and 10.35 Hz), 7.28 - 7.38 (1H, m), 7.55 (1H, dd, J 2.0 and 7.9 Hz), 8.0 (1h, broad s); MS (ES) *m/z* 575 (MH^+).

Example 181. Mutilin 14-[*N*-(Quinuclidin-3-oyl)carbamate]

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(quinuclidin-3-oyl)carbamate]

Quinuclidine-3-carboxylic acid was converted to the acid chloride hydrochloride by the procedure described in Example 161. This acid chloride was then reacted with (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (1.002 g) by the procedure outlined in Example 161 to yield the title compound as a colourless foam (1.116 g) after silica gel column chromatography; MS (ES) *m/z* 515 (MH^+).

Step 2. Mutilin 14-[*N*-(Quinuclidin-3-oyl)carbamate]

The product from Step 1, (1.13 g) in 1,4-dioxan (12 ml) was stirred at room temperature for 7 h with conc. hydrochloric acid (5 ml). The solution was then diluted with ethyl acetate and neutralized with saturated sodium hydrogen carbonate solution. The organic solution was washed with saturated sodium chloride solution, dried ($MgSO_4$) and evaporated to yield the crude product. After purification by silica gel chromatography, eluting with a gradient of 0-20% 9:1 methanol/35% ammonia solution in dichloromethane, the title compound was isolated as a white solid, (0.340 g). This solid, which was a mixture of two diastereoisomers, was digested in hot ethyl acteate and the resulting white solid was collected by filtration to yield one pure diastereoisomer of the title compound (0.140 g); ^{1}H NMR *inter alia* ($CDCl_3$) 0.75 (3H, d, J6.5 Hz), 0.90 (3H, d, J7.0Hz), 1.20 (3H, s), 1.40 (3H, s), 2.70-3.10 (5H, m), 3.20 - 3.42 (3H, m), 5.15-5.40 (2H, ddd), 5.70 (1H, d, J8.3Hz), 6.50 (1H, dd, J10.95, 17.4Hz) and 7.40 (1H, s); MS (ES) *m/z* 501 (MH^+). The mother liquors contained predominantly the other diastereoisomer of the title compound (0.200 g); ^{1}H NMR *inter alia* ($CDCl_3$) 0.75 (3H, d, J6.5 Hz), 0.90 (3H, d, J7.0Hz), 1.20 (3H, s), 1.41 (3H, s), 2.12 - 2.4 (3H, m), 2.70-3.10 (5H, m), 3.24 - 3.42 (3H, m), 5.15-5.45 (2H, m), 5.69 (1H, d, J8.3Hz), 6.50 (1H, dd, J11.0, 17.35Hz) and 7.40 (1H, s); MS (ES) *m/z* 501 (MH^+).

Example 182. Mutilin 14-{*N*-[(3*S*,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl]}-carbamate hydrochloride

A solution of mutilin 14-{*N*-[(3*S*,4*R*)-1-azabicyclo[2.2.1]hept-3-ylcarbonyl]}-carbamate (1.0 g; 2.06 mmol) in acetone (100 ml) was treated with 1M HCl in diethyl ether (4.2 ml; 4.20 mmol). The solution was stirred for 1 hour at room temperature and then concentrated *in vacuo*. The residue was triturated with diethyl ether to yield the title compound as a white solid (1.02 g, 95%); ν_{max} (KBr) 3421, 2924, 1772, 1734, 1704 and 1465cm^{-1}; ^{1}H NMR (D_2O) *inter alia* 0.62 (3H, d, *J* 6.0Hz), 0.90 (3H, d, *J* 6.9Hz), 5.22 (2H, dd, *J* 16.7, 11.1Hz), 5.61 (1H, d, *J* 8.1Hz), 6.35 (1H, dd, *J* 17.5, 11.1Hz).

Example 183. Mutilin 14-[*N*-(1-azabicyclo[3.2.1]octan-5-oyl)]carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-azabicyclo[3.2.1]octan-5-oyl)]-carbamate

Triethylamine (0.58 ml, 4.2 mmol) was added to a stirred mixture of racemic 1-azabicyclo[3.2.1]octane-5-carbonyl chloride hydrochloride (4 mmol), (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (668 mg, 2 mmol) and silver cyanate (600 mg) in dichloromethane (25 ml). The mixture was stirred overnight at room temperature, filtered and the filtrate evaporated to dryness. The crude product was purified by chromatography on silica gel, eluting with 35% ammonia solution:methanol:dichloromethane 1:9:90 to give the title compound as a white solid (480 mg), Rf 0.1; ^{1}H NMR ($CDCl_3$) *inter alia* 7.4 (1H, br s), 5.79 (1H, d, J 10), 3.21 (3H, s), 2.75-3.0 (6H, m); MS (+ve ion electrospray) m/z 515 (30%, MNH_4^+), m/z 556 (100%, M+H+MeCN$^+$).

Step 2. Mutilin 14-[*N*-(1-azabicyclo[3.2.1]octan-5-oyl)]-carbamate

The product of Step 1 (480 mg, 0.93 mmol) was dissolved in dioxan (2.5 ml) and conc hydrochloric acid (2.5 ml) was added slowly with cooling in an ice bath. The clear solution was stirred at room temperature for 4 hours and then diluted with water and basified by addition of sodium carbonate. The mixture was extracted with ethyl acetate and washed with brine. Drying ($MgSO_4$) and evaporation gave a crude product which was purified by chromatography on silica gel eluting with 35% ammonia solution:methanol:dichloromethane 1:9:90, giving two diastereoisomers of the title compound as a white solid (274 mg, 58%); Rf 0.08; ν_{max} ($CHCl_3$) 2962, 1772, 1736m, 1628 cm^{-1}; ^{1}H NMR ($CDCl_3$) *inter alia* 7.58 (1H, br s), 6.51 (1H, dd, J 17, 11), 5.75 (1H, d, J 8.4), 5.34 (1H, dd, J 11, 1.25), 5.19 (1H, d, J 17, 1.25), 3.36 (1H, br), 3.08-3.2 (1H,m), 2.7-3.05 (5H, m); MS (+ve ion electrospray) m/z 501 (100%, MH$^+$), MS (-ve ion electrospray) m/z 499 (100%, M- H$^-$).

Example 184. Mutilin 14-[*N*-(1-azabicyclo[2.2.2]octan-2-oyl)]carbamate

Step 1. (3*R*)-3-Deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin 14-[*N*-(1-azabicyclo[2.2.2]octan-2-oyl)]-carbamate

Triethylamine (0.2 ml, 1.5 mmol) was added to a stirred mixture of racemic 1-azabicyclo[2.2.2]octane-2-carbonyl chloride hydrochloride (ca 3 mmol), (3*R*)-3-deoxo-11-deoxy-3-methoxy-11-oxo-4-*epi*-mutilin (501 mg, 1.5 mmol) and silver

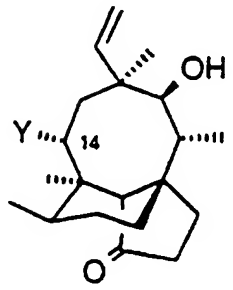
cyanate (225 mg) in dichloromethane (10 ml). The mixture was stirred overnight at room temperature, filtered and the filtrate diluted with dichloromethane and washed with aq sodium bicarbonate and with brine. Drying ($MgSO_4$) and evaporation gave a crude product which was purified by chromatography on silica gel, eluting with ethyl acetate: n-hexane 1:1. The title compound was obtained as a colourless gum (220 mg), Rf 0.12.

Step 2. Mutilin 14-[*N*-(1-azabicyclo[2.2.2]octan-2-oyl)]-carbamate

The product of Step 1 (200 mg) was dissolved in dioxan (2 ml) and conc hydrochloric acid (2 ml) was added slowly with cooling in an ice bath.. The clear solution was stirred at room temperature for 3 hours and then diluted with water and basified by addition of sodium bicarbonate. The mixture was extracted with ethyl acetate and washed with brine. Drying ($MgSO_4$) and evaporation gave a crude product which was purified by chromatography on silica gel eluting with 5% methanol in chloroform, giving two diastereoisomers of the title compound as a white foam (135 mg, 69%); Rf 0.08; ν_{max} ($CHCl_3$) 3309, 2946, 1780, 1735m, 1713 cm^{-1}; MS (+ve ion electrospray) m/z 501 (22%, MH^+), MS (-ve ion electrospray) m/z 499 (100%, M- H^-).

CLAIMS:

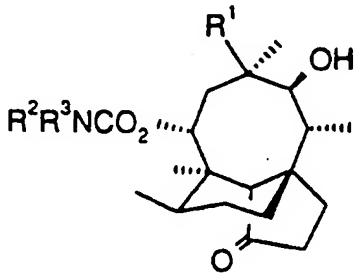
1. A compound of formula (1A) or a pharmaceutically acceptable salt or derivative thereof



(1A)

in which Y is a carbamoyloxy group, in which the N-atom is unsubstituted, or mono- or di-substituted.

2. A compound of general formula (3), or a pharmaceutically acceptable salt or derivative thereof



(3)

in which:

R^1 is vinyl or ethyl;

R^2 and R^3 are the same or different groups selected from

hydrogen;

a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group;

a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group;

an optionally substituted heterocyclic group;

an optionally substituted aryl group;

or together form an optionally substituted cyclic group of 3 to 8 ring atoms, optionally containing one additional heteroatom selected from N, O and S, and optionally fused to a hydrocarbon ring, a heterocyclic group or an aromatic group; or

R^2 is one of the above monovalent groups and R^3 is a group selected from SO_2R^4, COR^5, OR^5 and NR^6R^7 where

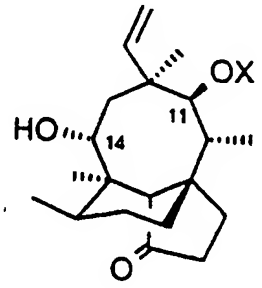
R^4 is selected from a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group; a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group; an optionally substituted heterocyclic group; an optionally substituted aryl group; an optionally substituted C_1 to C_6 alkylamino group; and an optionally substituted arylamino group;

R^5 is selected from hydrogen; a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group; a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group; an optionally substituted heterocyclic group; and an optionally substituted aryl group;

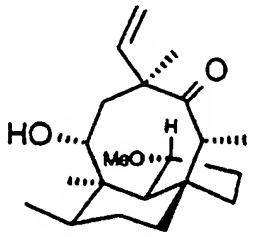
R^6 and R^7 are the same or different groups selected from hydrogen; a straight or branch chained, saturated or unsaturated, optionally substituted, C_1 to C_6 hydrocarbon group; a saturated or unsaturated, optionally substituted, C_3 to C_8 cyclic hydrocarbon group; an optionally substituted heterocyclic group, and an optionally substituted aryl group; or together form an optionally substituted cyclic group of 3 to 8 ring atoms, optionally containing one additional heteroatom selected from N, O and S, and optionally fused to a hydrocarbon ring, a heterocyclic group or an aromatic group.

3. A compound according to any preceding claim, substantially as hereinbefore described in any one of the Examples.

4. A method for preparing a compound of claim 1, which comprises reacting a compound of formula (4) where X is hydrogen or a hydroxyl protecting group, or a compound of formula (5) with an appropriately substituted carbamate-forming reagent



(4)



(5)

5. A process for the preparation of a compound according to claim 2, which comprises reacting a compound of formula (4) in which X is hydrogen or a hydroxyl protecting group, with

(a) a compound R^2NCO,

(b) a compound R^2R^3NCOCl, or

(c) phosgene or a chloroformate or a carbonate followed by a compound R^2R^3NH,

where R^2 and R^3 are as defined above and are protected where appropriate, and where necessary deprotecting the group X to generate a hydroxyl group at position 11, deprotecting a protected group R^2 or R^3, converting one group R^2 or R^3 to another group R^2 or R^3, or hydrogenating the vinyl group at position 12 to form an ethyl group.

6. A process for the preparation of a compound according to claim 2, which comprises reacting a compound of formula (5) with

(a) a compound R^2NCO,

(b) a compound R^2R^3NCOCl, or

(c) phosgene or a chloroformate or a carbonate followed by a compound R^2R^3NH,

where R^2 and R^3 are as defined above and are protected where appropriate, treating the product with an acid, deprotecting a protected group R^2 or R^3, converting one group R^2 or R^3 to another group R^2 or R^3, or hydrogenating the vinyl group at position 12 to form an ethyl group.

7. A pharmaceutical composition comprising a compound according to claim 1, 2 or 3, together with a pharmaceutically acceptable carrier or excipient.

8. A method of treating microbial infections in animals, especially in humans and in domesticated mammals, which comprises administering an antimicrobially effective amount of a compound according to claim 1, 2 or 3, or a composition according to claim 7, to a patient in need thereof.

9. Use of a compound according to claim 1, 2 or 3, in the preparation of a medicament composition for use in the treatment of microbial infections.

INTERNATIONAL SEARCH REPORT

Int onal Application No
PCT/EP 96/05874

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07C271/36 C07C271/64 A61K31/325 A61K31/33

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JOURNAL OF ANTIBIOTICS, vol. 29, no. 9, 1976, TOKYO JP, pages 923-927, XP002028938 H. EGGER ET.AL: "New pleuromutilin derivatives with enhanced antimicrobial activity, II" cited in the application see page 924 - page 925; table 1 -----	1

☐ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
7 April 1997	16.04.97

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Form PCT/ISA/210 (second sheet) (July 1992)